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THE ELEMENTS
OF
PATHOLOGICAL ANATOMY
AND
HISTOLOGY

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THE ELEMENTS

OF

PATHOLOGICAL ANATOMY AND HISTOLOGY

FOR STUDENTS

BY

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PREFACE

In placing this text-book before the elementary student I have tried to give him rather an insight into main types of pathological change than a description of numerous sub-varieties. This I have done in the belief that the teaching of principles governing variations is of more use, particularly in pathology, than the teaching of the names and appearances of numerous sub-varieties themselves.

Overlapping of the present volume with my 'Manual of General or Experimental Pathology' is inconsiderable, for in the following pages physiological considerations have been rigidly excluded. For this reason the two books will appeal to somewhat different classes of students.

All the illustrations have been specially drawn from Nature, under my own immediate supervision. Photography has not been used in making the microscopical drawings, because the interpretation of micro-photographs needs special training which the student has not had. On the other hand these drawings have been made by a non-medical artist, so that they represent faithfully the appearances seen by the elementary student when looking down the microscope, and are not semi-diagrammatic. The lack of resemblance between most drawings in text-books and corresponding sections given in class seems so great to students that the illustrations are often more of a hindrance than a help.

PART II

THE PATHOLOGICAL ANATOMY AND HISTOLOGY OF SPECIAL ORGANS AND TISSUES

SECTION PAGE

I. THE BLOOD 235

II. THE HEART AND PERICARDIUM 257

III. THE BLOOD-VESSELS AND LYMPHATIC VESSELS 295

IV. THE SPLEEN, THE LYMPHATIC GLANDS, AND THE THYMUS BODY . 318

V. THE BONES 329

VI. THE JOINTS, MUSCLES, TENDONS, AND BURSÆ 357

VII. THE VARIOUS PARTS OF THE DIGESTIVE TRACT—THE MOUTH AND NASO-PHARYNX 377

VIII. THE DIGESTIVE TRACT—(*cont.*) THE ŒSOPHAGUS AND STOMACH . . 395

IX. THE DIGESTIVE TRACT—(*cont.*) THE INTESTINES AND PERITONEUM . 409

X. THE LIVER AND BILE PASSAGES 443

XI. THE PANCREAS 478

XII. THE RESPIRATORY ORGANS 481

XIII. THE THYROID BODY 527

XIV. THE URINARY ONGANS 531

XV. THE ADRENAL BODIES 568

XVI. THE MALE GENERATIVE ORGANS 570

XVII. THE FEMALE GENERATIVE ORGANS 584

XVIII. THE MAMMARY GLAND 611

XIX. THE SKIN AND ITS APPENDAGES 623

XX. THE EYE AND EAR 637

XXI. THE NERVOUS SYSTEM 650

INDEX 695

LIST OF ILLUSTRATIONS

PLATES

PLATE

I. LARDACEOUS DISEASE OF KIDNEY . . . . *to face p.* 16

II. PIGMENTARY DEPOSITS . . . . ,, 26

III. MICRO-ORGANISMS IN BLOOD AND IN PYÆMIC ABSCESS . . ,, 56

IV. MICRO-ORGANISMS IN PUS . . . . ,, 68

V. TUBERCULOSIS . . . . ,, 106

VI. VARIETIES OF BLOOD CORPUSCLES . . . . . . ,, 244

VII. CRYSTALLINE DEPOSITS . . . . ,, 566

IN TEXT

FIG. PAGE

1. HYPERTROPHY OF LEFT VENTRICLE 6
2. DISUSE-ATROPHY OF TIBIA 7
3. HYPERPLASIA OF LYMPHOID TISSUE 7
4. HEMIAGENESIA OF VERTEBRA 8
5. EROSION OF THE BODIES OF VERTEBRÆ DUE TO AN ANEURYSM . . 9
6. FATTY INFILTRATION OF LIVER. OSMIC ACID 12
7. FATTY DEGENERATION OF CARDIAC MUSCLE. OSMIC ACID . . . 13
8. CLOUDY SWELLING OF KIDNEY 15
9. PIGMENT GRANULES IN NERVE CELLS. MARCHI'S FLUID . . . 27
10. SENILE GANGRENE OF TOE 30
11. HANDS FROM A CASE OF RAYNAUD'S DISEASE 31
12. CENTRAL CASEATION OF A TUBERCULOUS MASS 33
13. HYPOSTATIC CONGESTION OF THE PLEURA 41
14. FRACTURE OF COSTAL CARTILAGES REPAIRED BY BONE 79
15. HYPEROSTOSIS AROUND A SEQUESTRUM OF FEMUR 80
16. CHRONIC INFLAMMATION OF OMENTUM 81
17. FORMATION OF NEW BLOOD-VESSELS 85
18. SECTION OF GRANULATING ULCER 96
19. GRANULATION-TISSUE CELLS 97
20. A MILIARY TUBERCLE 106
21. TUBERCULOUS CARIES OF THE LOWER END OF THE TIBIA . . . 108
22. SECTION OF A LUPOID ULCER 109

FIG. PAGE
23. SYPHILITIC CARIES OF SKULL 113
24. GUMMATA OF LIVER 114
25. SECTION OF EARLY SYPHILOMA OF MYOCARDIUM 115
26. SECTION OF MADURA FOOT 117
27. SECTION OF VENULE SHOWING COMMENCING THROMBOSIS . . . 127
28. ANÆMIC INFARCT OF SPLEEN 134
29. SECTION OF A CORN 159
30. SECTION OF A FIBROMA 162
31. SECTION OF A NASAL POLYPUS 164
32. SECTION OF A CAPILLARY ANGEIOMA 170
33. SECTION OF VENOUS ANGEIOMA 171
34. SECTION OF GLIOMA 173
35. SECTION OF RHABDOMYOSARCOMA 175
36. SECTION OF LEIOMYOMA 176
37. SECTION OF TUBULAR ADENOMA OF THYROID 180
38. SECTION OF PAPILLARY ADENOMA 181
39. SECTION OF SEBACEOUS ADENOMA 182
40. SEBACEOUS ADENOMA. PORTION OF SEPTUM BETWEEN ADJACENT CAVITIES 183
41. SECTION OF 'INTESTINAL POLYPUS' (PENDULOUS TUBULAR ADENOMA) . 184
42. LARGE ROUND CELL SARCOMA INVADING LUNG 187
43. SPINDLE-CELL SARCOMA 189
44. SECTION OF MYELOID SARCOMA 191
45. PSAMMOMA 194
46. SECTION OF ALVEOLAR SARCOMA 195
47. SECTION OF CHONDRO-SARCOMA 196
48. SECTION OF OSTEO-SARCOMA 198
49. SECTION OF ENDOTHELIOMA 201
50. SECTION OF SQUAMOUS-CELL CARCINOMA 209
51. 'CELL NESTS' AND PRICKLE CELLS FROM A SQUAMOUS-CELL CARCINOMA 211
52. SECTION OF RODENT CANCER 213
53. SECTION OF COLUMNAR-CELL CARCINOMA 216
54. SECTION OF PAPILLOMATOUS CYSTADENOMA 218
55. SECTION OF SPHEROIDAL-CELL CARCINOMA (SOFT PART) . . . 221
56. SECTION OF SPHEROIDAL-CELL CARCINOMA (HARD OR 'SCIRRHOUS' PART) 222
57. SECTION OF SPHEROIDAL-CELL CARCINOMA (GROWING EDGE) . . 223
58. SECTION OF COLLOID CARCINOMA 224
59. SECTION OF WALL OF PAPILLIFEROUS OVARIAN CYST 229
60. SECTION OF WALL OF DERMOID CYST 232
61. PERICARDITIS 258
62. SECTION OF ORGANISING PERICARDITIS 261
63. SECTION OF AORTIC VALVE WITH VEGETATIONS 267

FIG. PAGE
64. VEGETATIVE ENDOCARDITIS 268
65. VEGETATIVE ENDOCARDITIS 269
66. ULCERATIVE ENDOCARDITIS 270
67. CHRONIC ENDOCARDITIS 274
68. SECTION OF MYOCARDITIS 281
69. SECTION OF MYOCARDIUM SHOWING CHRONIC FIBROSIS . . . 288
70. SOFT ATHEROMA OF FEMORAL ARTERY 298
71. SACCULAR ANEURYSM OF ARCH OF AORTA 302
72. SECTION OF SYPHILITIC ENDARTERITIS (ENDARTERITIS OBLITERANS) . 308
73. SECTION OF TUBERCULOUS ARTERITIS 309
74. PORTION OF VARICOSE SAPHENA VEIN 311
75. CASEOUS TUBERCULOUS MASS IN SPLEEN 320
76. EARLY TUBERCULOSIS OF LYMPHATIC GLAND 324
77. OSTEOMALACIA OF FEMUR 331
78. CARIES OF PHALANGES 333
79. SEPTIC OSTEOMYELITIS 334
80. SYNOSTOSIS 338
81. EARLY CARIES OF VERTEBRA 339
82. BONE IN RICKETS 342
83. SECTION OF BONE IN RICKETS 343
84. SCURVY RICKETS 345
85. OSTEITIS DEFORMANS. OUTER SURFACE OF TIBIA 347
86. OSTEITIS DEFORMANS. INNER SURFACE OF TIBIA 347
87. LEONTIASIS, VAULT OF SKULL 350
88. PERIOSTEAL SARCOMA OF FEMUR 353
89. ENDOSTEAL SARCOMA OF TIBIA 354
90. MYELOID (ENDOSTEAL) SARCOMA OF LOWER JAW 355
91. SECTION OF PAROTID TUMOUR 393
92. MALIGNANT DISEASE OF ŒSOPHAGUS 396
93. SIMPLE CHRONIC GASTRIC ULCER 400
94. MALIGNANT DISEASE OF STOMACH (CARDIAC END) 403
95. TYPHOID ULCER WITH SLOUGH ATTACHED 417
96. TUBERCULOUS ULCER 419
97. GANGRENOUS APPENDICITIS 421
98. DYSENTERIC ULCERATION OF RECTUM 423
99. MALIGNANT STENOSIS OF COLON 429
100. 'NUTMEG' LIVER (CHRONIC VENOUS CONGESTION) 444
101. LARDACEOUS LIVER 447
102. PYLEPHLEBITIC ABSCESS OF THE LIVER 455
103. MULTILOBULAR OR ATROPHIC FIBROSIS OF THE LIVER . . . 459
104. MULTILOBULAR FIBROSIS OF LIVER (POST-SYPHILITIC ?) 461
105. SECTION OF INTERCELLULAR FIBROSIS OF LIVER (CONGENITAL SYPHILIS) 464
106. ADENOMA OF THE LIVER 466

FIG. PAGE
107. PRIMARY SPHEROIDAL-CELL CARCINOMA OF LIVER 467
108. SECONDARY NODULES OF CARCINOMA IN LIVER 468
109. INTRA-HEPATIC GALLSTONES 472
110. CARCINOMA OF LIVER COMMENCING ROUND A GALLSTONE . . . 474
111. TUBERCULOUS DISEASE OF LARYNX 483
112. SYPHILITIC ULCERATION OF LARYNX 484
113. MALIGNANT ULCERATION OF LARYNX 487
114. SECTION OF CARNIFIED LUNG 494
115. SECTION OF LUNG SHOWING VESICULAR EMPHYSEMA 495
116. SECTION OF CROUPOUS PNEUMONIA 500
117 SECTION OF BRONCHO-PNEUMONIA 504
118. SECTION OF BRONCHO-PNEUMONIA 505
119. SUPPURATIVE BRONCHO-PNEUMONIA 508
120. GANGRENE OF LUNG 510
121. SECTION OF FIBROID LUNG 512
122. CASEOUS MILIARY TUBERCULOSIS OF LUNG 515
123. EXTREME CASEOUS TUBERCULOSIS OF LUNG 516
124. TUBERCULOSIS OF LUNG WITH EXCAVATION 517
125. CALCIFICATION OF PLEURITIC ADHESIONS 525
126. SECTION OF KIDNEY SHOWING ACUTE TUBAL NEPHRITIS . . . 538
127. SECTION OF CONTRACTED WHITE KIDNEY 540
128. CONSECUTIVE NEPHRITIS 542
129. CALCULOUS PYONEPHROSIS 544
130. TUBERCULOUS KIDNEY 545
131. CHRONIC FIBROSIS OF KIDNEY (CHRONIC GRANULAR KIDNEY) . . 547
132. SARCOMA OF KIDNEY 550
133. HYDRONEPHROTIC KIDNEY, FROM A CHILD 552
134. PORTION OF VILLOUS PAPILLOMA OF BLADDER PASSED IN URINE . . 557
135. CONGENITAL CYSTIC DISEASE OF KIDNEY 560
136. SECTION OF KIDNEY SHOWING CONGENITAL CYSTIC DISEASE . . . 561
137. ADRENAL BODY FROM A CASE OF 'ADDISON'S DISEASE' . . . 568
138. TUBERCULOUS TESTIS (OPENED FROM BEHIND) 574
139. GUMMATA OF TESTIS 575
140. SECTION OF RETAINED TESTICLE 577
141. HÆMORRHAGIC SARCOMA OF TESTIS 578
142. FIBROCYSTIC DISEASE OF THE TESTIS 579
143. PROSTATIC ENLARGEMENT WITH VESICAL CHANGES 582
144. SECTION OF CHRONIC ENDOMETRITIS (HYPERPLASTIC OR CATARRHAL VARIETY) 589
145. SECTION OF CHRONIC ENDOMETRITIS (POLYPOSE VARIETY) 590
146. UTERUS SHOWING MULTIPLE FIBRO-LEIOMYOMATA 593
147. MALIGNANT DISEASE OF THE BODY OF THE UTERUS 594
148. PYOSALPINX 597
149. A MULTILOCULAR OVARIAN CYST 601

FIG. PAGE
150. SECTION OF DECIDUOMA MALIGNUM 607
151. SECTION OF BREAST SHOWING CHRONIC MASTITIS 613
152. SECTION OF TUBULAR FIBRO-ADENOMA OF BREAST 615
153. SECTION OF ACINOUS FIBRO-ADENOMA OF BREAST BECOMING CARCINOMATOUS 616
154. FUNGATING MALIGNANT ULCER OF BREAST 618
155. GALACTOCELE ('BUTTER-CYST') 620
156. DUCT PAPILLOMA OF BREAST 621
157. SECTION OF SKIN IN NEIGHBOURHOOD OF AN INFLAMMATORY FOCUS . 624
158. SECTION OF ŒDEMATOUS SKIN (SCROTUM) 627
159. CEREBRAL ABSCESS (TEMPORO-SPHENOIDAL LOBE) 664
160. CEREBRAL TUMOUR 668
161. LACERATION OF BRAIN (TRAUMATIC) 672
162. CEREBRAL HÆMORRHAGE 673
163. SECTION OF SPINAL CORD IN A CASE OF TRANSVERSE MYELITIS . . 676
164. SECTION OF SPINAL CORD BEING INVADED BY SARCOMA OF SPINAL MENINGES 678
165. SECTION OF SPINAL CORD SHOWING SCLEROSIS OF POSTERO-MEDIAN COLUMNS 680
166. SECTION OF SPINAL CORD IN INFANTILE PARALYSIS 682
167. SECTION OF SPINAL CORD SHOWING HYDROMYELIA 684
168. SECTION OF HYPOGLOSSAL NERVE FROM A CASE OF HEMIATROPHY OF THE TONGUE 687
169. SECTION OF HYPOGLOSSAL NERVE FROM A CASE OF HEMIATROPHY OF THE TONGUE 687
170. SECTION OF AMPUTATION NEUROMA 691
171. VAGUS NERVES FROM CASE OF RECKLINGHAUSEN'S DISEASE . . . 692

Errata

Page 53, line 3 from bottom, *for* Plate V *read* Plate VI
,, 57, lines 8, 11, and 15 from top, *for* Plates IV and V *read* Plates III and IV
,, 250, line 13 from top, *for* in the case of *read* including
,, 250, ,, 29 ,, *after* found *add* and only in æstivo-autumnal fever
,, 319, ,, 21 ,, *after* corpuscles *add* or of fibrous tissue

PATHOLOGICAL ANATOMY
AND
HISTOLOGY

INTRODUCTION

Pathology is that branch of medical science which treats of the changes undergone by the tissues and functions in disease. It falls naturally into two divisions—(1) that which concerns the description of the macroscopic and microscopic alteration of diseased tissues, and (2) that which endeavours to correlate those changes with the alterations in function that we meet with in disease. Pathology, therefore, may be regarded either from an anatomical or from a physiological point of view. We are further rapidly learning that it has to be also considered from a chemical point of view.

In the present volume it is only the anatomical aspect of Pathology that will be considered, and this will be dealt with in two parts. In the first part pathological changes generally will be considered both macroscopically and microscopically. This branch of the subject is often spoken of as 'general pathological anatomy and histology,' to distinguish it from that which is concerned with the various changes occurring in the individual organs and tissues of the body, and which is usually termed 'special pathological anatomy and histology.' The latter will form the second part of our subject.

All the changes we shall have to describe concern cells or the products of the life-history of cells. It is therefore clear that if we could possess a full knowledge of the pathological changes that are undergone by cells of different kinds, we should possess a full knowledge of pathological anatomy and histology. As a matter of fact, our knowledge of the changes that are undergone by individual cells is extremely small; our information is principally derived from observation of collections of cells. It is true that in some cases we are not hindered by this fact, as, for example, when we assert, from consideration of the epithelial cells of the thyroid body, that the colloid change is one which affects epithelial cells. But in other cases much difficulty is introduced, because cells of different kinds are closely intermingled to build up the structure of a single tissue. Thus we know that the lardaceous change chiefly affects the middle coats of the arterioles, but since the middle coat of the arterioles consists of muscle fibres, fibrous tissue, capillaries, to mention only three constituents, it becomes a matter of the greatest difficulty to decide whether the lardaceous change consists in the presence of something deposited locally but brought from a distance, or whether it is an alteration of certain of the cells constituting the middle coat, and if so, which are the elements affected.

In spite of the fact, therefore, that anatomy and histology are subjects in which it might be supposed that accurate observation would give final information, this is not absolutely the case. However carefully a given diseased structure is examined, one always arrives at a point at which it has to be confessed that there is room for difference of opinion. That this should be so is rendered the more certain in that no two examples of a single pathological process are absolutely identical in appearance, which is tantamount to saying that the number of factors at work in the production of a given result is so great that it is almost, if not quite, impossible to find another exactly similar combination.

This point has a very important application in connection with pathological anatomy and particularly with pathological histology. If we examine a dozen different sections from a dozen different, but normal, human lungs, we find that the general appearances are so similar in all of them that they may, for practical purposes, be said to be identical. Moreover, if a specimen from a thirteenth normal lung be placed beneath the microscope, we shall be able to say, after a single glance, that the tissue is pulmonary. But supposing that we take a dozen sections from a dozen different cases of the pulmonary disease known as pneumonia, we shall probably find that no two of them are exactly similar, that some of them differ from others so considerably that it is difficult to conceive that they are all examples of the same disease, and that all of them are so different from normal lung that it is hard to believe that they are lung at all.

The reason for this variability is partly the enormous variation in the actual changes which go to make up the disease 'pneumonia,' but partly it lies in the fact that the histological appearances of the affected lung differ from time to time. That is to say, the disease has different *stages*, and the appearances differ to a considerable extent according to the stage in which the lung was at the time at which it was obtained for microscopical examination. Thirdly, the appearances differ according as the lung was or was not normal before it became the seat of pneumonia. It may previously have been the seat of some inflammation or other change which has altered its constitution so considerably that the pneumonic process is not an uncomplicated one. And innumerable other possibilities might be mentioned which are of very frequent occurrence.

It therefore comes about that the very greatest care must be taken in the examination of a specimen before an opinion is pronounced upon the nature of the change by which it is affected. This is equally true, whether we are considering macroscopic or microscopic specimens. Nevertheless, it is usually in the case of microscopic sections that the difficulty is most felt by the student who has but just left the examination of normal tissues. And yet there is no more fatal bar to the attainment of a good knowledge of pathological histology than that of attempting to 'spot' sections.

Lastly, it is necessary to have a clear recognition of the value of pathological anatomy and histology. It is of course possible that we may regard them as ends in themselves, being content with a recognition of the different forms under which disease shows its effects. But it is clear that a far more important use of the facts we obtain is, to regard them as the basis for consideration of the processes which bring them about, and the alterations in function which they themselves induce. It is well to know the histological appearances of the different varieties of cancer, for example, but it is far better not to stop here, but to pass on to the examination of cancer as a disease, and consider how its manifestations in the patient are to be explained by means of the knowledge we have obtained. In a word, pathological anatomy and histology find their great importance in the basis which they afford for the interpretation of symptoms and signs met with at the bedside.

PART I

GENERAL PATHOLOGICAL ANATOMY AND HISTOLOGY

SECTION I

THE RETROGRADE CHANGES

Under this name are included a number of processes which differ greatly in respect of the appearances which they produce in the tissues they affect, and in the causes which bring them about. They have this in common, however, that they all arise from interference with the nutrition of the tissues, and therefore are all in the direction of death. In some cases the change itself consists in the actual occurrence of local death and cannot be recovered from, in others it appears as if the change consists more in the deposition of a substance at some point which has been formed elsewhere (infiltration), while in yet a third class the proteid material breaks up into substances which are of a simpler chemical constitution (degeneration).

(1) ATROPHY AND HYPERTROPHY

Strictly speaking, under the general terms 'atrophy' and 'hypertrophy' are included several different conditions. Thus, it is not accurate to speak of atrophy unless a part has at one time reached its full adult dimensions, and has subsequently diminished in size; it may be smaller than normal because it has, owing to insufficient nutrition, failed to reach the normal, or because there has been some congenital peculiarity in the cells from which it sprang. The same, *mutatis mutandis*, is true of hypertrophy.

However considerable the macroscopic changes may be in cases of atrophy and hypertrophy, microscopic changes are, as a rule, very slight, and they may be quite unrecognisable, or even the principal change may be evidenced in quite another direction

Nothing, for example, can be more striking than the hypertrophy that occurs in the left ventricle in cases of chronic fibrosis of the kidney (fig. 1), and yet the microscope reveals nothing abnormal in the cardiac muscle itself. So, too, when a tibia is atrophied from disuse of the limb owing to disease of the ankle, knee, or hip-joint (fig. 2), the bone itself shows few microscopic changes. The cancellous tissue may be a little more extensive than usual, or the Haversian canals a little wider, but that is all.

The fact is that in these instances (and they are typical of the great majority) there has been, in the one case, a new formation of muscle elements in every respect similar to those of the normal heart, and in the other instance a removal of portions of formed bone. This diminution in size (tibia) is, further, not the true converse of the condition in which the tissue reaches an abnormally great size (heart) ; the true converse is clearly one in which the tissue elements, though individually of normal size, are numerically fewer than normal.

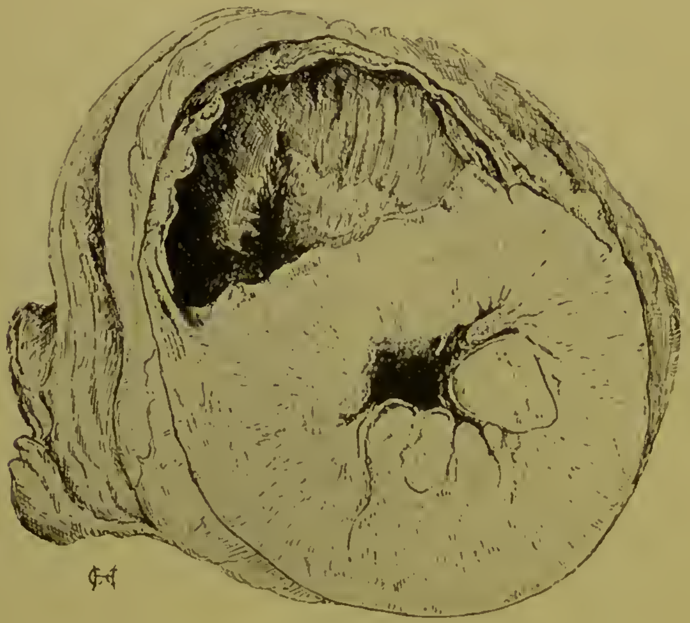


FIG. 1.—HYPERTROPHY OF LEFT VENTRICLE. × $\frac{4}{5}$.

The ventricles have been divided midway between the apex of the heart and the base, and are looked at from below. From a case of chronic renal fibrosis.

For these reasons the terms which refer to the sizes of organs and tissues are defined more exactly. Where a part is larger than normal because it consists of a greater number than usual of elements which are in other respects quite normal, it is agreed to speak of the existence of **hyperplasia** (fig. 3). Where the elements, though of normal size, are present in too small numbers, the condition is known as **hypoplasia** or **aplasia**. This leaves the terms **hypertrophy** and **atrophy** to signify, respectively, conditions in which the constituent elements of the part, after having reached normal proportions, advance still further, or retire. **Agenesia** (fig. 4) and **gigantism** are terms which have been introduced to denominate insufficient growth and excessive growth, respectively, when they depend upon some congenital peculiarity. Unfortunately, however, it is still customary to use the terms ‘hypertrophy’ and ‘atrophy’ loosely in the macroscopic senses of ‘abnormally large’ and ‘abnormally small.’

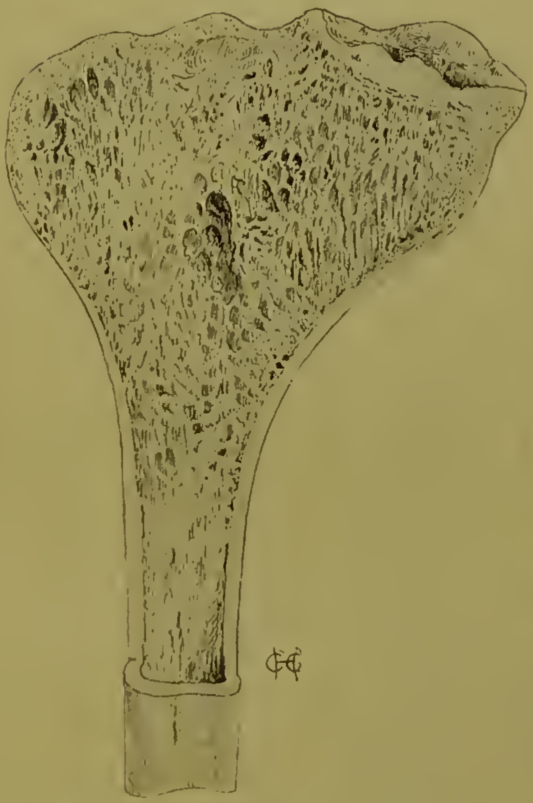


FIG. 2.—DISUSE-ATROPHY OF TIBIA. × $\frac{2}{3}$.
The shaft is thinner and the cancellous tissue is looser than normal. The condition in this instance depended upon old tuberculous disease of the knee.

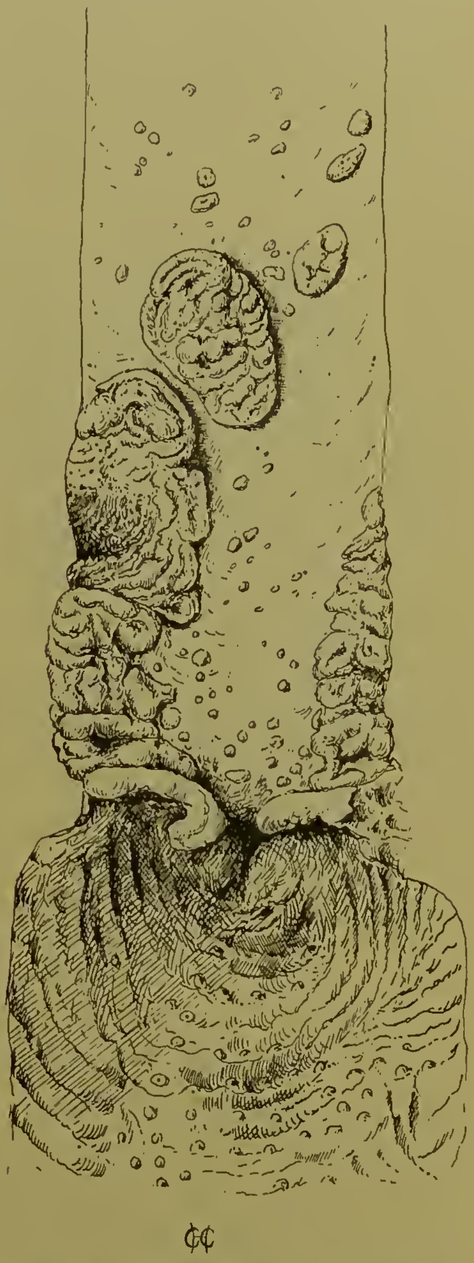


FIG. 3.—HYPERPLASIA OF LYMPHOID TISSUE. × $\frac{3}{4}$.
Small and large intestine about the ileo-cæcal valve of an infant who died of summer diarrhœa.

Hyperplasia is undoubtedly far more common than hypertrophy, and atrophy than hypoplasia. Perhaps the best example of a true hypertrophy is seen in the case of the muscle cells of the uterus during pregnancy, when the individual cells may reach to eleven times their normal length in the unimpregnated state of the organ. Hypertrophy of the cells does not, however, account entirely for the increased size of the uterus at term, for hyperplasia of muscle cells also occurs. The best example of pure uncomplicated atrophy is perhaps found in the case of the ganglion cells of the brain in old age; they simply become smaller and the pigment in them becomes more obvious. Pure hypoplasia is well seen in the case of limbs that fail to reach their normal size owing to the occurrence of those changes in the nervous system which constitute acute anterior poliomyelitis (infantile paralysis), and in the aorta in some cases of chlorosis. As a rule, however, atrophy is not uncomplicated, but is accompanied by some other changes of which fibrosis is by far the most common. Indeed, a combination of atrophy with fibrosis is the commonest of all retrogressive changes, and is invariably found in some tissue or other in old age. 'Midgets' and 'giants' are examples of agenesia and gigantism respectively, but these conditions need not of necessity affect the whole body; localised affections of the kind are not excessively rare.

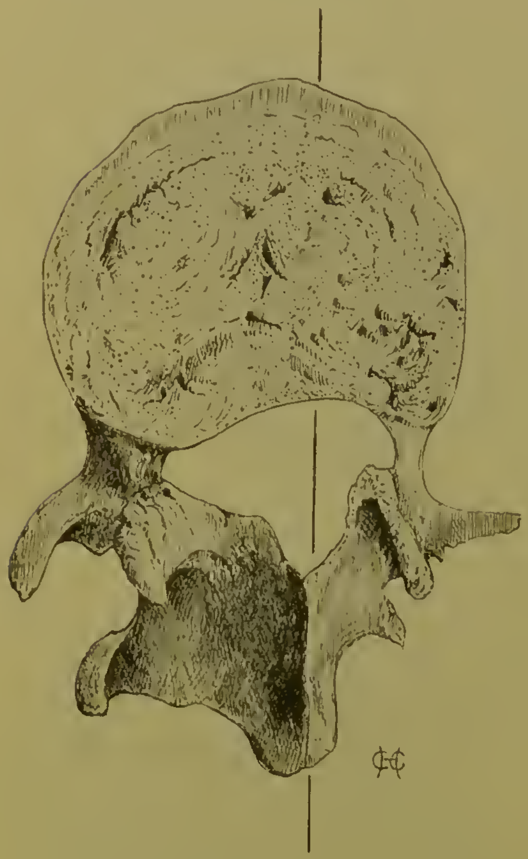


FIG. 4.—HEMIAGENESIA OF VERTEBRA. × $\frac{3}{4}$.

The entire right half of the bone is smaller than the left. The condition involved the left half of the body and the right cerebral hemisphere. A vertical line is drawn to show that there is curvature of the bone to the left in addition.

It is necessary to distinguish between hypertrophy, or hyperplasia, and a condition known as **pseudo-hypertrophy**. Pseudo-hypertrophy is found in association with paralysis in the condition known as pseudo-hypertrophic muscular paralysis, but though the limbs and certain muscles are undoubtedly increased in girth, this is due to an increase of fat in the intermuscular septa alone;

so far from being hypertrophied or hyperplastic, the muscles themselves are greatly atrophied.

The chief causes of pathological atrophy are *pressure, disuse, and removal from nervous control.* Pressure atrophy accounts for that disappearance of tissue which takes place in the immediate neighbourhood of a new-growth or an aneurysm (fig. 5). It is very largely dependent upon a diminution in the amount of blood occasioned by the pressure. Mere disuse is undoubtedly a cause of atrophy, just as use is a cause of hypertrophy and hyperplasia. The umbilical vein after birth, being no longer used to convey blood to the fœtus from the placenta, becomes atrophied into a fibrous cord, and persists as the round ligament of the liver. So, too, when the muscles of a limb cease to be of use owing to fixation of the joint by disease, they undergo atrophy. The atrophy in this case is not, however, uncomplicated, for the muscular bundles that remain show as a rule very marked fatty degeneration in addition. Atrophy from disuse is very frequently associated with atrophy from removal of nervous control, but the two conditions are not identical. There is no doubt that the large multipolar cells in the anterior cornua, for example, not only exert some nutritive influence upon the axons to which they give rise, but, in addition, influence the nutrition of the muscular cells with which those axons are in communication at their distal ends by their terminal arborisations.

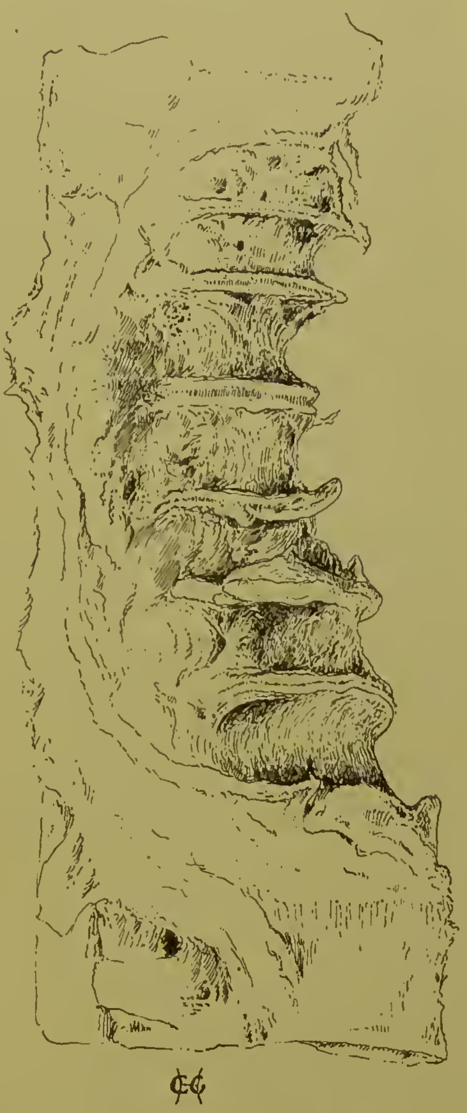


Fig. 5.—Erosion of the Bodies of Vertebræ due to an Aneurysm. × ¾.

(From the St. George's Hospital Museum.)

A condition that may fairly be included amongst the atrophies is that general emaciation that accompanies so many diseases, and particularly those in which fever is a prominent symptom. The atrophy principally affects fat, but the proteid elements of the body do not escape. Thus, the pectoral muscles in phthisis are thin and pale and often exhibit marked fatty degeneration, the heart is almost invariably small, and the other tissues show similar changes, excepting that in them the processes have not, as a rule, gone so far. Here, the wasting is due to the fact that the febrile process has led to an abnormally large destruction of tissue. In cases of stenosis of the œsophagus there is also an extreme emaciation, but this is due to the fact that the local condition does not allow the food to reach the stomach. In diabetes mellitus there is extreme wasting, but the appetite is greatly increased, and an abnormally large amount of food is taken. The explanation of the wasting in this disease is not quite clear, but it must be remembered that the essential feature of the disease is the elimination of a substance—sugar—in the urine, which has an extremely high nutritive value. Moreover, pulmonary tuberculosis is a common complication of diabetes mellitus, and though diabetes, of itself, and in spite of the absence of fever, leads to great wasting, the degree of that wasting is enhanced if the fever of pulmonary tuberculosis becomes superadded.

The emaciation which accompanies malignant disease is in part, no doubt, due to the fact that a large portion of the food taken into the body is applied to the uses of a tissue that is physiologically outside the body, but it is also probably due to the fact that the metabolism of the tumour adds something to the blood which exerts a deleterious influence upon nutrition at large.

(2) THE FATTY CHANGE

The fatty change is probably the commonest and the widest spread of all pathological processes. It affects every kind of tissue, though some kinds with greater frequency than others; it is especially apt to affect cells, in this respect its tendency being exactly similar to its tendency in physiological conditions. The fatty change may be so widespread as to be macroscopically obvious, or it may, though affecting a tissue such as the heart in an extreme degree, be so finely disseminated that its existence is only recognised after staining with osmic acid.

When the fatty change is so extensive as to be macroscopic, the mass of fat so formed may be generally distributed over the body (constituting general 'lipomatosis' or 'obesity'), or it may be accumulated into a definite mass (constituting a 'lipoma' or 'fatty tumour'); but both of these conditions come more strictly into the class of New-growths and will not be considered here. Nevertheless fat may be deposited in macroscopic quantities, and under pathological conditions which do not come into this category. The change is then closely akin to the physiological deposition of fat. Thus, the heart may be completely overladen with fat, but since the sub-pericardial areolar tissue is one which normally contains a certain amount of fat, we are obliged to regard the excessive deposit as being pathological merely by way of an excess of a normal state. So, too, fat may be deposited in the liver in quantities so large that the weight of the entire organ is markedly increased, that a section is greasy to the eye and to touch, and that the normal reddish-brown colour is replaced by an ochrey yellow; and here, again, the fat is in a situation in which fat is normally present, so that this variety of fatty liver may reasonably be regarded as an example of the normal which has gone to excess.

Besides the conditions which have been referred to above, the presence of fat droplets is to be recognised at times in situations from which it is normally absent. Thus, they may be found in the muscle-cells of the heart, in the epithelial cells of the convoluted tubules of the kidney, in endothelial cells of blood-vessels, and so on. It is clear that the explanation that sufficed to explain the other variety of fatty change will not suffice here. We have here a definitely pathological process which has no exact counterpart, though it may have analogies, in physiology.

Now, of both of these processes we have examples in physiological life. The deposition of fat which has been taken up by the intestinal villi after a meal rich in fat, in the cells of the liver, is nothing more than an infiltration of the hepatic cells. And the deposition of fat droplets in the sub-pericardial and intermuscular connective tissues is of exactly the same kind. In the formation of milk, on the other hand, a different process is at work. In this case we have a distinct breaking down of protoplasm into fat, and the other form of fatty change occurring in pathology has here its counterpart.

We have then to recognise two varieties of fatty change, (a) fatty infiltration, (b) fatty degeneration. The two forms may coexist in a given case, but nevertheless they are fundamentally different in their mode of origin.

Of these two forms of fatty change, infiltration is of far the less clinical importance; fatty degeneration, indeed, being one of the most serious of morbid processes. At times it is quite easy to distinguish between fatty infiltration and fatty degeneration, but in the majority of cases the distinction can only be made with difficulty, and in many instances a definite opinion is impossible. This is especially the case when the fatty change affects a tissue that is normally the seat of fatty infiltration, e.g. the liver. It is true that fat deposited in the liver under normal circumstances, as also when there is fatty infiltration as a morbid process, is deposited in the periphery of the lobule, owing to the fact that it is brought thither by the branches of the portal vein (fig. 6); but when the amount of fat in the lobule thus deposited is very great, it may involve the entire lobule and become indistinguishable from a condition in which the protoplasm of the hepatic cell has extensively degenerated into fat. Where the tissue does not normally contain fat the matter is much simpler, for the vast probability is that the case is one of degeneration. Thus, when the heart is the seat of fatty change (fig. 7), one has only to determine whether the process involves the muscular fibres themselves, or whether it is restricted to the intermuscular septa, to decide that one has to deal with a case of fatty degeneration in the first instance or of fatty infiltration in the second. This same instance affords a good example of the relative importance of the two conditions, for it is manifest that it will

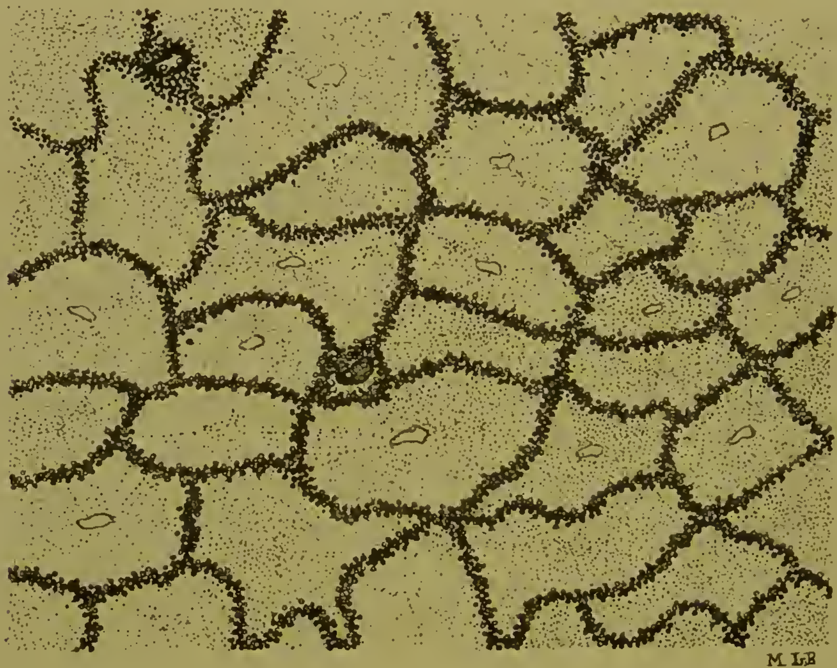


FIG. 6.—FATTY INFILTRATION OF THE LIVER. OSMIC ACID. × 40.
From a case of early tuberculosis of lung. The fat globules are regularly arranged around the lobules.

far less concern the heart's efficiency as a pump if there is an excess of intermuscular fat than if a considerable portion of the cardiac muscle itself is replaced by fat.

Another point which is often of use when endeavouring to decide between fatty infiltration and fatty degeneration is the size of the droplets of fat. In fatty infiltration the droplets are as a rule much larger than in fatty degeneration, and are liable to be more irregular in size; in fatty degeneration they are as a rule minute and of equal size throughout. Nevertheless, even in fatty infiltration the droplets are at first minute, though they tend to rapidly run together and coalesce to form drops of considerable size. The difference between the two forms is also well shown if microscopic sections are made and are treated with alcohol, which, of course, removes the fat. In the case of fatty degeneration little or no difference is noticed between a section thus prepared and one which has not been treated with alcohol at all; but in the case of fatty infiltration circular spaces are recognisable everywhere, and these indicate the former situation of fat drops.

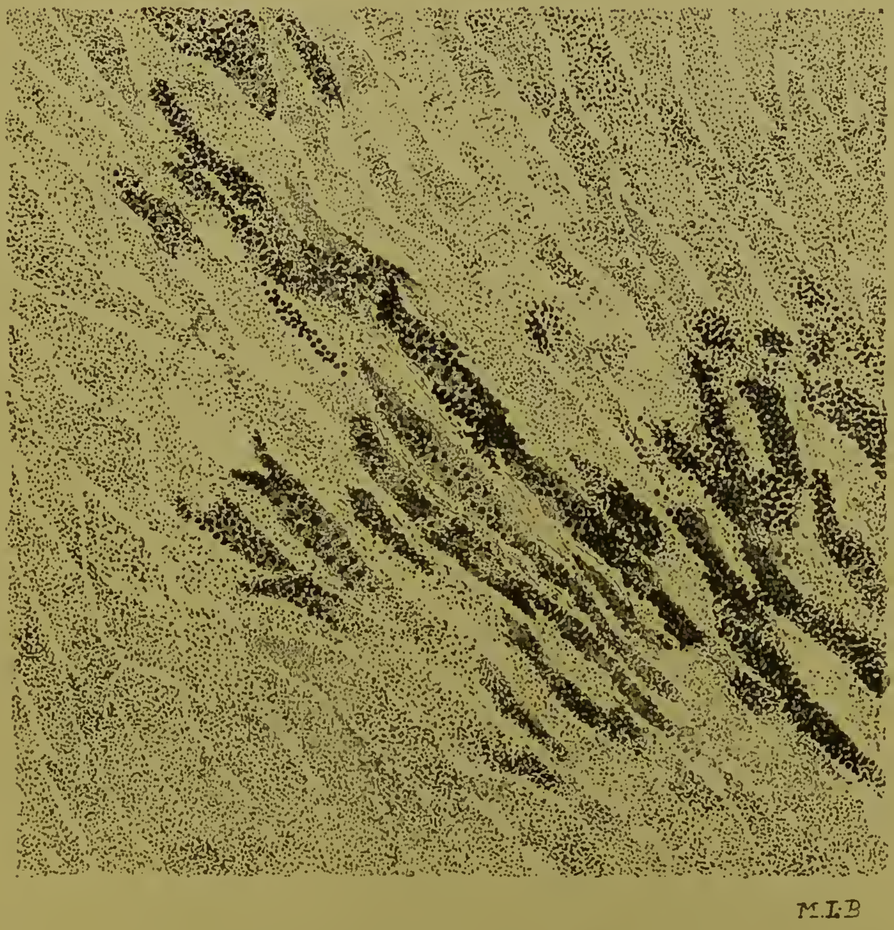


Fig. 7.—Fatty Degeneration of Cardiac Muscle. Osmic Acid. × 420.

It must not be supposed that the essential elements of a part which is the seat of fatty infiltration are totally unaffected. If the fatty infiltration is of limited extent, and particularly if it has not been of long duration, the essential elements may, on removal of the fat, recover their normal size and revert to their normal function completely; but if this removal of the infiltrated fat does not take place, the essential elements undergo pressure-atrophy. How considerable the atrophy may be, may be seen in the case of an ordinary fatty liver, sections of which have been treated with alcohol. The section appears to be a mere spongy network, and is hardly recognisable as liver; it is only upon careful examination that the attenuated remains of the liver cells are distinguished.

It is not only the normal elements of the body that are liable to become fatty; these changes may also occur in truly pathological materials. Thus, a pus cell is frequently fatty, and the new growths of all descriptions are prone to the change, while inflammatory tissue often becomes fatty, especially if the cause of the inflammation be either the B. tuberculosis or the virus of syphilis. So, too, proliferated endothelial cells are liable to undergo the change, as is shown by the constancy with which the fatty (or rather the closely allied caseous) change is seen in atheroma.

Fatty degeneration is of regular occurrence wherever a part is disused. Thus it is found in muscle and bone of a limb that has been cut off from its nervous supply, and plays a considerable part in converting the now useless tissues into a form of substance that is easy of absorption and elimination; the medullary sheaths of the nerves themselves in the limb also break down into the same substance and are removed.

(3) CLOUDY SWELLING

Cloudy swelling is a change that is practically only met with in cases in which the fatal illness has been accompanied by fever. Thus it is seen in all cases where death has arisen from one of the acute specific fevers.

Macroscopically, a tissue affected with cloudy swelling looks as if it had been boiled. It is somewhat larger than normal, semi-opaque, and as a rule pale in colour. Microscopically, the cells of which it is composed are swollen, their outlines ill-defined, their protoplasm hyaline and almost granular. The change principally affects cells, and in particular the cells of the liver, kidney, and heart; but sometimes connective-tissue fibres undergo a modification which is either identical or, at least, is closely similar. Though the protoplasm of the cells is profoundly altered, the nuclei are commonly distinct in their outline; hence the change can hardly be mistaken for any other morbid condition.

The change is certainly not a fatty one, for treatment of the material with ether or alcohol does not clear up the granular appearance in the cells, neither do the minute granules stain black with osmic acid. Nevertheless, it is probably a stage on the way to the formation of fat, since diseases which, when acute, are accompanied by cloudy swelling, when chronic, are liable to be accompanied by fatty changes (probably fatty degeneration) in the same regions. The connection of this change with the other metamorphoses is, at present, quite uncertain; in particular, it is unknown what relation it has with the hyaline change which it resembles in so many respects.

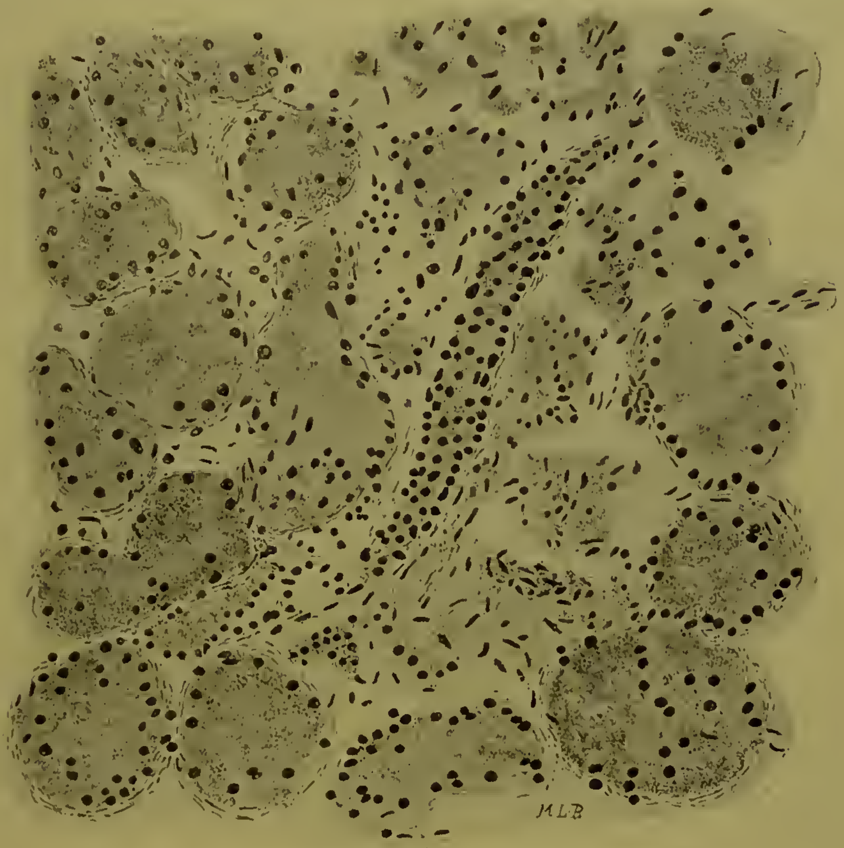


Fig. 8.—Cloudy Swelling of Kidney. × 420.
A section of the cortex. From a case of acute lobar pneumonia.

It is uncertain whether we are to regard cloudy swelling as a degeneration or as an infiltration. In any case, we are certain that the change is one of proteid material. It has been asserted that it is possible for a tissue which has been affected with cloudy swelling to recover completely, but this is open to doubt.

(4) THE LARDACEOUS CHANGE

The lardaceous, amyloid, or waxy change affects almost entirely the middle coats of the smaller arteries. It consists in the presence, in these situations, of a hyaline, almost translucent material (lardacein), which is really of proteid composition, though it differs in certain respects, and in particular in the fact that it is very resistent to peptic digestion, from the ordinary proteids met with in the body. It is uncertain whether the change is a degeneration or an infiltration—that is to say, whether a metamorphosis takes place in the situations in which the lardacein is ultimately found, or whether a substance which is locally converted into lardacein is first of all laid down in the arterial walls, and there subsequently undergoes change; or whether, in the third place, lardaceous material is formed as such in the other tissues or blood, and is locally deposited in the fully formed state. All organs and tissues do not exhibit the same tendency to be affected by the lardaceous change; thus, the spleen, the liver, the kidneys, are the commonest situations in which the modification is found, and even though it may be widely dispersed throughout the body, it is always in these organs that it is most extensive and pronounced.

Lardacein has certain staining characteristics; it yields a mahogany brown with a solution of iodine in potassium iodide, whereas the unaffected tissues stain a canary yellow, and it takes on a brilliant rose colour with gentian violet (Plate I); both of these reactions are quite characteristic. Other staining reactions, as, for example, that with iodine green, are noteworthy, but less characteristic.

It has been said above that the lardaceous change is commonly found to involve the middle coats of the smaller arteries, but it is questionable whether this situation is the only one in which it occurs. Some authors have maintained that it also involves epithelial cells. Thus it has been described as occurring in hepatic cells and in the epithelium of the renal convoluted tubules, and when the change is met with in the stomach or in the intestine, it certainly appears as if the gland cells themselves shared in the process. When the spleen is affected, the lardaceous

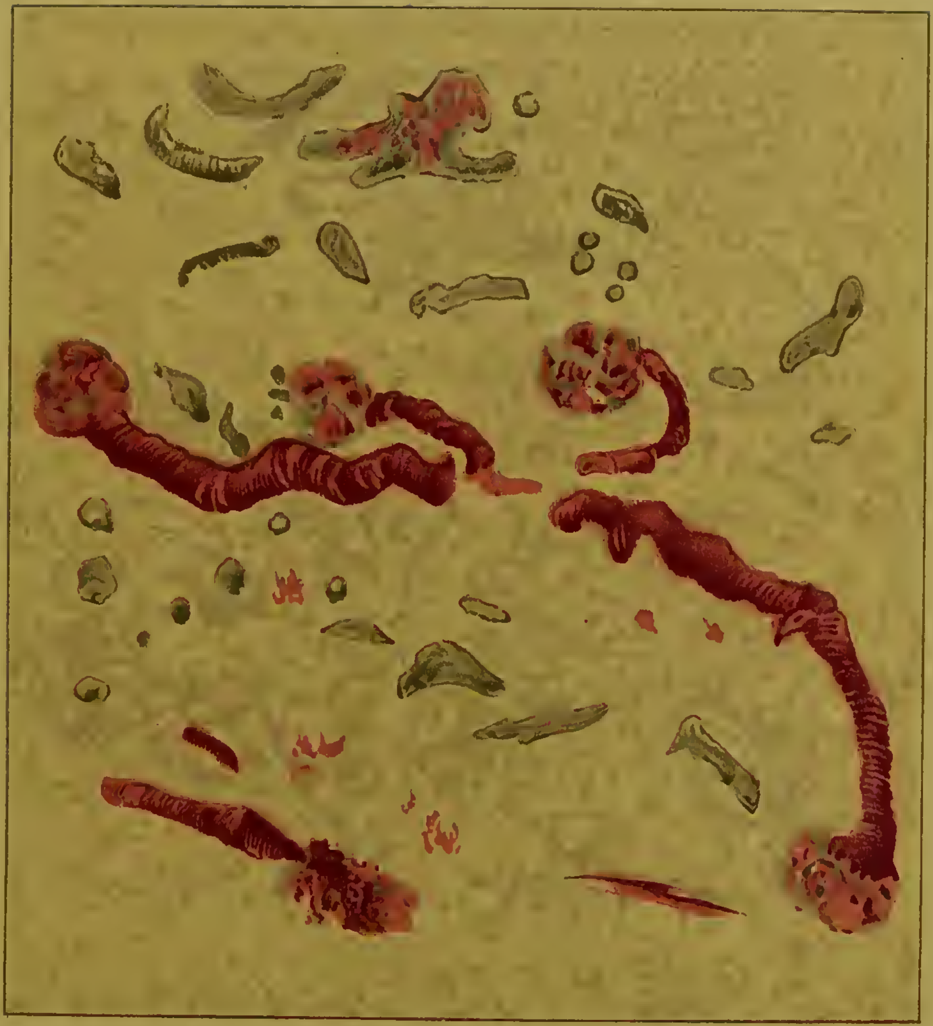
PLATE I

Section of a kidney, showing an advanced stage of lardaceous disease. Stained with anilin-methyl-violet, washed in saturated oxalic acid solution, mounted in cane-sugar syrup. Magnified 420 diameters.

The lardaceous material is stained bright red, and is seen to affect the vessels exclusively, and of these only the arterioles and parts of the glomerular tufts. The lardaceous modification of the circular muscular coat of the arterioles is distinct.

The lardaceous disease in the case from which the specimen was obtained followed upon syphilis unattended by suppuration.

Plate I.



Lardaceous Disease of Kidney.

change may show itself in two very different forms; in the majority of cases it involves the malpighian corpuscles, and these, becoming larger and semi-translucent, cause the organ to assume the appearance known as 'sago spleen;' in other cases the vessels in the interstitial fibrous trabeculæ are affected, and the organ, though somewhat enlarged, is not altered in so remarkable a manner.

The causes of the lardaceous change are chiefly two, viz. suppuration and syphilis. Of these two causes, suppuration is undoubtedly the more frequent and important, and syphilis in many instances leads to lardaceous disease by way of the suppuration that syphilitic bone disease so commonly induces. But there is equally no doubt that syphilis, quite apart from suppuration, is, in a minority of cases, the sole effective agent. For some reason that is not at present understood, when lardaceous disease affects the interstitial vessels in the spleen, the previous history of the case has almost always been one of syphilis uncomplicated by suppuration. Probably the commonest disease upon which the lardaceous change is superadded is pulmonary tuberculosis, but this only means that pulmonary tuberculosis, with its attendant suppuration, is an excessively common disease.

The lardaceous change, from the very widespread nature of its incidence in the body, leads to a well-marked and usually very obvious series of anatomical changes, and a collection of symptoms so definite as to constitute a definite 'disease.' The patient with lardaceous disease is usually a somewhat pallid individual, often, however, bearing a rosy complexion, and has, at times, a peculiar 'satiny' skin. He will probably pass a somewhat large quantity of pale urine containing a considerable quantity of albumen, will be likely to suffer much from diarrhœa, and perhaps also from frequent vomiting. The reasons for these disturbances are amply explained by the occurrence of the pathological alteration of the kidney, the mucous membrane of the intestine, and of the stomach. He will also be liable to suffer from attacks of syncope, for the alteration of the blood-vessels, together with the alteration of the blood itself which the vascular changes induce, leads to a profound modification of the nutrition of the heart. The earliest date which can be with certainty ascribed to the onset of lardaceous disease, after the onset of the original disease upon which the lardaceous disease itself depends, is three weeks. Once developed, it is doubtful whether it ever recedes.

(5) THE MUCOID CHANGE

The mucoid change consists in a transformation of a tissue or some elements of a tissue into mucus, and is very widespread. It may affect whole tracts of tissue, or it may affect only a few cells here and there ; it may involve epithelial cells or connective-tissue cells in all their numerous varieties ; it may form a definite type of tissue resembling Whartonian jelly, and of this may form a true tumour (myxoma), or it may involve a tumour of quite another type, and thus help to form the very large class of mixed tumours (myxo-sarcoma, fibro-myxoma, &c.). Of all kinds of tissue in the body, the members of the connective-tissue group are the most liable to undergo mucoid change, and in them not only the cells but also the intercellular substance may be affected.

The mucoid change is a true degeneration. The proteid element which undergoes the change is altered entirely, and cannot revert to its original constitution. Though in certain respects like proteid, in the majority it is totally dissimilar. It is, however, closely allied with the nucleo-proteids, differing from them principally in the fact that, after treatment with dilute sulphuric acid, mucin yields a substance which reduces copper from its solutions, whereas the nucleo-proteids, when treated in the same way, yield no reducing substance. Mucin, or rather a closely allied substance known as ‘paramucin,’ is frequently found in large quantities in cysts, especially those of the ovary.

Owing to the large quantity of water which it holds, tissues which have undergone the myxomatous or mucoid change, shrink very considerably if they are exposed to the action of alcohol. For this reason, if the true nature of the change is to be understood, it is necessary to examine sections that have not been hardened in any dehydrating solution. The best plan is to harden in 5 per cent. formalin, to cut by the freezing method straight from the formalin solution, stain, and mount direct in Farrant's medium. If a true myxoma prepared in this way be examined, a number of delicate cells with scanty cell-protoplasm, but with numerous and long fine processes, will be seen in all parts of the field. Between the processes is a homogeneous substance which stains a rosy pink with van Gieson's stain. This is the true mucoid material. It varies in amount in different cases, but is always a very prominent feature of the specimen. In a tissue that has undergone mucoid degeneration, true myxomatous cells are, of course, absent, and the picture is one in which parts of the original tissue over a greater or a less extent are replaced by the homogeneous mucoid.

Where a tissue which has undergone mucoid degeneration is treated with alcohol during its preparation (e.g. is embedded and finally mounted in Canada balsam), it presents the appearance of a very delicate meshwork of connective tissue, in which the presence of nuclei is hard to make out. The difference between sections of a nasal myxoma prepared after the two fashions is such that it is difficult to believe that both were derived from the same mass of tissue.

The formation of an excessive amount of mucus by a mucous membrane constitutes a condition which has numerous analogies with mucoid degeneration, but which can hardly be included in the class of degeneration; it is rather an example of an excessive performance of a normal function. It occurs in cases where a mucous membrane is the seat of inflammation, or even of irritation, and gives to the fluid that exudes from the blood-vessels certain peculiar characters. Thus, pus derived from a mucous surface is 'stringy' and tenacious, and becomes 'ropy' on addition of a caustic alkali. Whether this peculiarity of the pus is due to the presence in it of mucus alone, is a different question; there is reason, in fact, to believe that it is in part due to the presence of nucleo-proteid derived from the pus cells themselves.

(6) THE COLLOID CHANGE

The colloid change affects epithelium alone, and, as far as our knowledge goes, is, in the strictest sense of the term, a degeneration. Physiologically, it occurs in the thyroid gland, but this is the only region in which it can be said to be normal. Pathologically, it occurs in a great many situations. Thus, it is found as a prominent or the sole constituent of the contents of cysts, whether of the thyroid (cf. fig. 37), the kidney, the ovary, or the testis, in a considerable number of cases. It occurs also as a degenerative change in certain forms of new-growth, notably in the carcinomata. Amongst the carcinomata it seems to affect only the varieties arising from spheroidal (cf. fig. 58) and columnar cells; colloid degeneration of a squamous cell carcinoma is unknown. When the change concerns a mass of spheroidal or of columnar carcinoma, it may be found in any part of the body subject to these varieties of growth, but it is particularly liable to affect carcinomata of the stomach, intestines, or peritoneum;

carcinoma of the breast or of the pancreas, however, at times, is found to have undergone this particular degeneration.

Colloid material, when viewed in mass, is a tenacious semi-opaque substance, often colourless, but often yellow or red or brown from admixture of altered blood-pigment. Under the microscope it appears to be homogeneous, or at most faintly granular. When acted upon by alcohol it shrinks (though not to the same extent as mucin), becomes definitely granular, and often arranges itself in irregular bands or strands. From this property microscopic sections in which there is a considerable amount of colloid are apt to become irretrievably wrinkled in preparation for mounting in Canada balsam; it is far better to omit the use of alcohol altogether, and to mount the specimen in Farrant's medium, after having hardened the material itself in 5 per cent. formalin and cut by the freezing method.

The degree to which a given specimen may show the colloid change is very variable. It may be confined to a cell here and there, or it may affect the tissue so universally that no vestige of a cell remains. As a rule, however, the condition lies between these two extremes; in some places of the same section masses of cells which have undergone no degeneration will be found, in others there will be collections of colloid in which no cells are visible, and elsewhere cells and colloid will be found intermixed.

As a rule, it is only more or less chronic forms of pathological material that undergo colloid degeneration, so that when it affects a carcinoma, for example, it is not a carcinoma of a rapidly growing kind or one that attains to a very large size; nevertheless, colloid carcinoma of the stomach or peritoneum may be very voluminous and of extremely rapid growth.

Though in many respects like some of the other degenerative changes, colloid may be distinguished by a peculiar staining reaction with a mixture of picric acid and acid fuchsin (rubin) in watery solutions and in equal parts (van Gieson's stain). When acted on by this stain colloid is tinted a reddish orange; hyaline material under the same conditions becomes a pale pink, and mucoid a bright rose-red.

(7) THE HYALINE CHANGE

The hyaline change is a form of degeneration that was described by von Recklinghausen as occurring in connective tissue. It manifests itself by a swelling of the connective-tissue fibrils, which also become semi-translucent and hyaline in appearance. There is some doubt as to the nature of this particular change, and especially as to whether it is identical with, or different from, the 'fibrinoid' change described by Neumann. Ernst, however, has attempted to give precision to the term 'hyaline' by showing that van Gieson's stain gives, with certain substances that might fairly be said, from their macroscopic appearances, to be 'hyaline,' a flesh-pink colour, thereby differentiating them from colloid and mucoid substances, which in many instances are indistinguishable from them to the naked eye. A further difficulty is introduced by the fact that the term 'hyaline' has already been appropriated in the case of certain morbid products found in the renal tubules in cases of nephritis; judged by Ernst's standard these are not hyaline at all, for they do not stain a flesh-pink with van Gieson's stain, but a rosy red. Neumann's 'fibrinoid' degeneration is by many competent authorities considered to be nothing more than an œdematous condition of the connective-tissue fibrils themselves, and certainly with van Gieson's stain it yields a colour identical with that given by ordinary connective tissue.

The great point upon which von Recklinghausen relied in differentiating hyaline from colloid and mucoid degenerations is the fact that the chemical reactions of the three substances are different. It was not asserted that even hyalin itself is always of one and the same chemical constitution; probably, indeed, there are several kinds of hyalin.

There is no doubt that van Gieson's stain will, at times, differentiate between substances that with other stains appear to be identical; and this, too, in one and the same section. But it must be confessed that van Gieson's stain is at times, and for no known reason, capricious, and even then it is very uncommon for a tissue that has been stained with it to show foci where the colour is a flesh-pink. From this it may perhaps be inferred that the hyaline change is not a very common one, a conclusion which is supported by other considerations.

(8) THE VITREOUS CHANGE

The vitreous change, or 'Zenker's degeneration,' is not very often seen. It shows itself as a translucent modification with local enlargement of various muscular bundles, in some one or other anatomical muscle of a patient who has died from a highly febrile and exhausting disease. Thus, a likely situation in which to find it is the rectus abdominis muscle of a patient who has died of typhoid fever, but it may also be present in the diaphragm or in the muscles of the limbs. In any case, it is a modification of voluntary, as distinguished from involuntary, muscle. It may be produced experimentally by freezing the living muscle, or by injuring it after death and before the establishment of rigor mortis. The change has many analogies with coagulative necrosis, and with the other changes in which a more or less translucent material is present; but whether it is identical with one or other of these changes it is, at present, quite impossible to say. Certainly, in the seats of incidence of the vitreous change there is the most marked difference from other forms of degeneration.

(9) CALCIFICATION

Calcification is a process which is actually normal in a considerable number of situations in the body. It is normal in the growth of bone throughout the entire period of youth, and may fairly be termed normal in that calcification which is found almost invariably in the costal cartilages of persons of advanced years. As a matter of fact the calcification of costal cartilages in old age is typical of the same change when it affects tissues as a morbid process. Just as the calcareous infiltration of the costal cartilages does not in every case develop at one and the same age, so the morbid calcareous change occurs now in old, now in young persons. Nevertheless the tissue in which calcification occurs is always itself, so to speak, senile. That is to say, calcification never occurs in young and vigorous tissues, but always in tissues the nutrition of which is feeble, or in which nutrition has ceased altogether; in a word, calcification takes place in dying or dead tissues, and in such tissues alone.

The calcium salts deposited in calcification are principally the phosphate and carbonate; salts, therefore, identical with those laid down in the formation of bone. They are carried to the part where they are deposited by the blood-vessels, and it is one of the most remarkable points in reference to calcification, whether normal or pathological, that it is especially met with where the blood supply is marked by an extraordinary poverty. Thus, a fœtus which has escaped into the abdominal cavity, and which has in consequence died, may become so densely impregnated with lime salts as to merit the name 'lithopædion,' or the centre of a dense uterine fibroid which is almost devoid of blood-vessels may become converted into a mass of stone upon which neither knife nor saw will make the faintest impression.

As a morbid process, calcification occurs in the most diverse situations. It is met with in lungs and bronchial glands, in the middle and internal coats of arteries, as in atheroma, in the encapsulating walls that are liable to be formed around foreign bodies of all kinds (e.g. hydatid cysts), in whatever part of the body they may be found, in new growths, particularly those in connection with the periosteum and those of very slow growth and ill supplied with blood, in the laryngeal and other cartilages in old age, in the nerve cells of the brain, in pleural adhesions (fig. 125), and elsewhere. In all these situations the method whereby the condition builds itself up is identical. It consists in the deposition of minute grains of lime salts which are arranged in no order. At first these are separated from one another by fairly wide intervals, but later they become closely packed together. These processes can, at times, be recognised well in the large ganglion cells of the brains of old persons ; when present the ganglion cells have a peculiar mulberry-like appearance that cannot well be mistaken for anything else.

While the fully developed calcareous change cannot fail to be recognised, it is not always easy to recognise its earliest manifestations. In this connection, the fact that granules of calcium salts seem to have a special affinity for hæmatoxylin and its derivatives is often of considerable use. A microscopic section throughout which calcium salts are deposited, when stained with one of these dyes, generally looks as if it had been carelessly prepared ; in particular, it looks as if an excess of the stain had been left in the section and had become deposited because tap-water had been used instead of distilled water. The most careful preparation, however, fails to do away with the deposit, and experience shows that it is situated in the region where the calcium salts are aggregated, and that it can be prevented from making its appearance by steeping the section for a short time in a dilute solution of some mineral acid before staining, a process which dissolves out the calcium salts.

(10) THE PIGMENTARY CHANGES

Pathological pigmentation may depend upon the deposition of pigments derived from substances formed in the body, or from substances derived from outside. They may therefore be either **intrinsic** or **extrinsic**. The intrinsic pigments may further be differentiated according as they are either hæmatogenous or non-hæmatogenous.

The hæmatogenous pigments are, of course, derived from hæmoglobin, but in the course of its retrograde metamorphoses hæmoglobin does not always form one and the same substance. In particular, it may or may not lose the iron which it holds in combination, and further that iron may maintain the characters it possesses in hæmoglobin, or it may revert to a less complicated form. When iron is combined with globulin to form hæmoglobin, the metal is said to be ‘masked,’ in that the ordinary tests applied by the chemist for the detection of iron no longer manifest its presence. One of the first changes that occur in the downward metamorphosis of hæmoglobin is the conversion of this ‘masked’ iron into the ordinary variety. The pigment thus formed is called **hæmosiderin**. At a still later stage in the change the blood pigment loses its iron, and an iron-free pigment known as **hæmatoidin** is produced.

Hæmosiderin is a far commoner pathological pigment than hæmatoidin. It is said to be the cause of that greenish discolouration of the abdominal walls which indicates commencing decomposition after death, the sulphuretted hydrogen which is produced in the intestines combining with the iron of the hæmosiderin derived from the hæmoglobin that has escaped from the abdominal blood-vessels after death.

Hæmosiderin is also formed in all cases where there has been marked hæmolysis, e.g. in pernicious anæmia, in malaria, and in certain forms of poisoning. It may then be found in any of the tissues, but is especially liable to be present in the hepatic cells. In pernicious anæmia in particular it may be found in large quantities, and its existence may be clearly demonstrated if the tissue or section be treated with dilute hydrochloric acid and ferrocyanide of potassium. The iron under these circumstances is precipitated as Prussian blue. The iron is always found in the cells, and as a rule the affected cells occupy the intermediate or outer zone of the lobule (Plate II, A). As a macroscopic change, iron may usually be well demonstrated in the kidney in cases of pernicious anæmia, but, for some reason which is not clear, its microscopic demonstration is rarely so clear in the renal cells as in those of the liver.

The commonest situation in which hæmatoidin is found is old blood-clots in the brain. The substance is crystalline as a rule, but it may also be found in a granular form. When crystalline it forms minute rhombic plates of a yellow or orange colour. It is probable that hæmosiderin cannot be formed without the agency of living cells, but that they are unnecessary to the formation of hæmatoidin.

Other hæmatogenous pigments found pathologically in the tissues, and closely allied with those we have just been considering, are those present in jaundice and derived from the bile. The bright yellow colour of the skin and other tissues in recent jaundice is probably due to the presence of bilirubin, and possibly also to choletin; the olive-green colour that characterises jaundice of long standing is almost certainly due to the presence of biliverdin. In ordinary cases of jaundice bile pigment is present in the tissues in a state of solution, but under certain circumstances—e.g. in icterus neonatorum—it may be found in the form of crystals.

Pigmentation around the sites of former chronic inflammation and congestion are chiefly hæmatogenous, but in part they are due to an excessive formation of the pigment which is normally present in some degree in the deepest layers of the epidermis in all but albinos, and which, by its presence in extremely large quantities in the skin of the negro, accounts for his characteristic colour.

Certain forms of pathological pigmentation depend essentially upon an increase of the pigment normally present in the deeper layers of the epidermis. Thus, in most cases of Addison's disease there is an increased pigmentation in situations that are exposed or are subject to pressure. In other morbid conditions—e.g. vitiligo—there are localised patches at which there is a deficiency of the normal pigment, with the result that the skin is, in these regions, abnormally white.

In the case of one variety of new-growth (melanotic sarcoma) the formation of pigment is an essential and characteristic feature. The pigment may be in large quantity or small, it may be intensely black or of the faintest yellow, and variations between these wide limits may be found in different parts of one and the same tumour; but whatever the precise features of the specimen, it invariably shows certain cells in which the presence of pigment can be recognised (Plate II, C). Melanotic sarcoma is not uncommon, but another form of sarcoma is known which is excessively rare, and which, from its character of appearing of a dull, or in some cases a bright, green, has been termed a 'chloroma.' In the case of chloromata it is doubtful whether the colour is due to a definite pigment formed by the cells of the tumour itself, or whether it is due to the refraction of light by crystals of fat in the cells. The latter is the more probable explanation, and derives support from the fact that the green colour is lost if the tissue be treated with alcohol. The pigment in melanotic sarcomata is called *melanin* and contains no iron, but contains sulphur.

Other forms of pathological pigmentation with intrinsic pigments occur in the heart, the intestine, and the large nerve cells of the brain and cord. In the case of the heart and the intestine, pigment is not normally present, but a pale yellow or brownish pigment appears to be a normal constituent of the large cells of the nervous system.

When the heart becomes the seat of pathological pigmentation the granules of pigment are deposited in the muscle fibres at either end of the nucleus (Plate II, B). This pigment is present in considerable quantities and causes the heart to take on a brown appearance, which is quite recognisable with the naked eye. Since, in addition, the organ is always atrophied, the morbid condition is known as 'brown atrophy of the heart.' It is quite unknown whether this change has any special significance, and we are equally ignorant as to the source of origin of the pigment.

In the case of the intestine a senile pigmentation is known which has many analogies with brown atrophy of the heart; it is rarely recognisable, however, with the naked eye. The pigment lies in the muscular coat. Another form of pathological pigmentation of the intestine affects the mucous coat. It occurs in a few cases of Addison's disease, and is, no doubt, quite comparable with the pigmentation of the skin and buccal mucous membrane.

In the case of the large cells of the nervous system, the presence of pigment is normal, but an alteration in the amount or the arrangement of the pigment appears to be one of the first indications of morbid changes of the most varied kinds (fig. 9).

Extrinsic pigments are of the most various kinds. The commonest is carbon, which is found in the lungs and bronchial

PLATE II

Fig. A.—Section of liver from a case of pernicious anæmia, showing Quincke's siderosis. Stained with alum-carmine, treated with dilute hydrochloric acid and potassium ferrocyanide, mounted in Canada balsam Magnified 420 diameters.

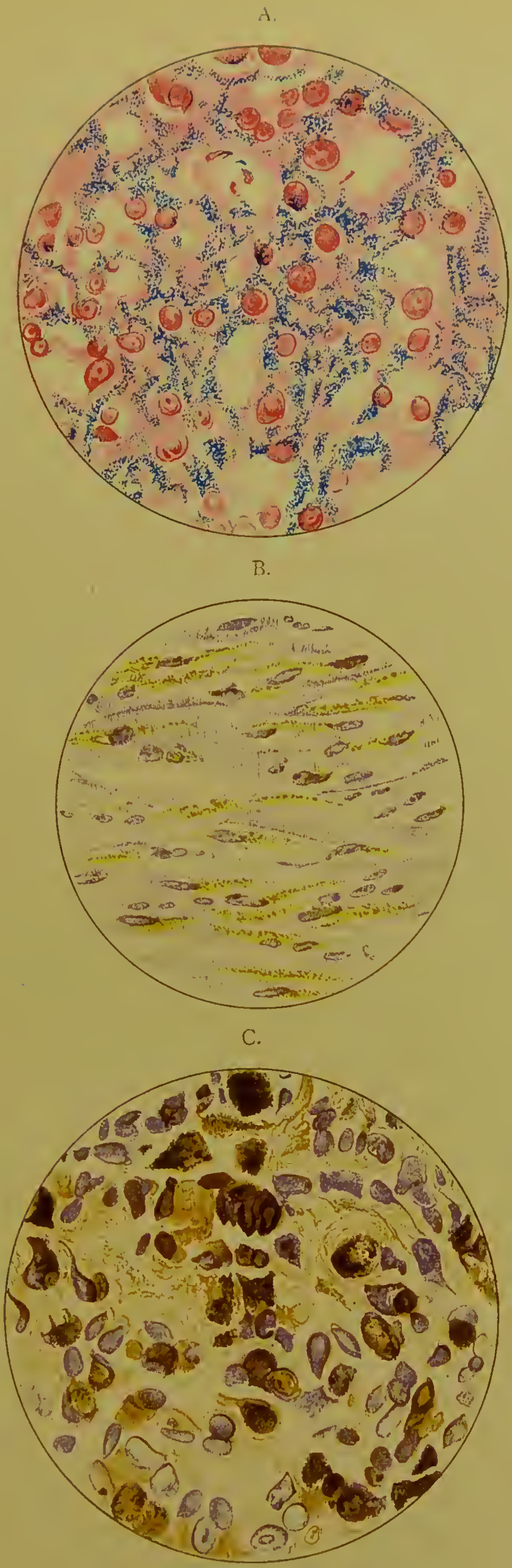
The 'unmasked' iron is seen deposited in the hepatic cells in the form of Prussian blue.

Fig. B.—Section of myocardium showing brown atrophy. Faintly stained with hæmalum, mounted in Farrant's medium. Magnified 420 diameters.

The pigment is of its natural colour, and shows a special tendency to be arranged at the poles of the nuclei of the cardiac muscle.

Fig. C.—Section of melanotic sarcoma. Stained with hæmalum, mounted in Canada balsam. Magnified 420 diameters.

The section shows the sarcoma cells to be of diverse shape, as indicated by the shapes of the nuclei. Certain of the cells are filled with a deep brown pigment, which entirely obscures the details of the cell. In other cases the pigment is lighter, while many cells show a complete absence of pigment.



Pigmentary Deposits.

glands of all who have lived any length of time in cities or large towns where coal is used as a fuel. The condition is known as 'anthracosis.' Another pigment sometimes found in the lungs (but not nearly so commonly as was at one time the case) is red oxide of iron. It occurs among the knife-grinders of Sheffield. Stonemasons, too, frequently present a peculiar slatey appearance of the lungs due to the inhalation of minute particles of stone.

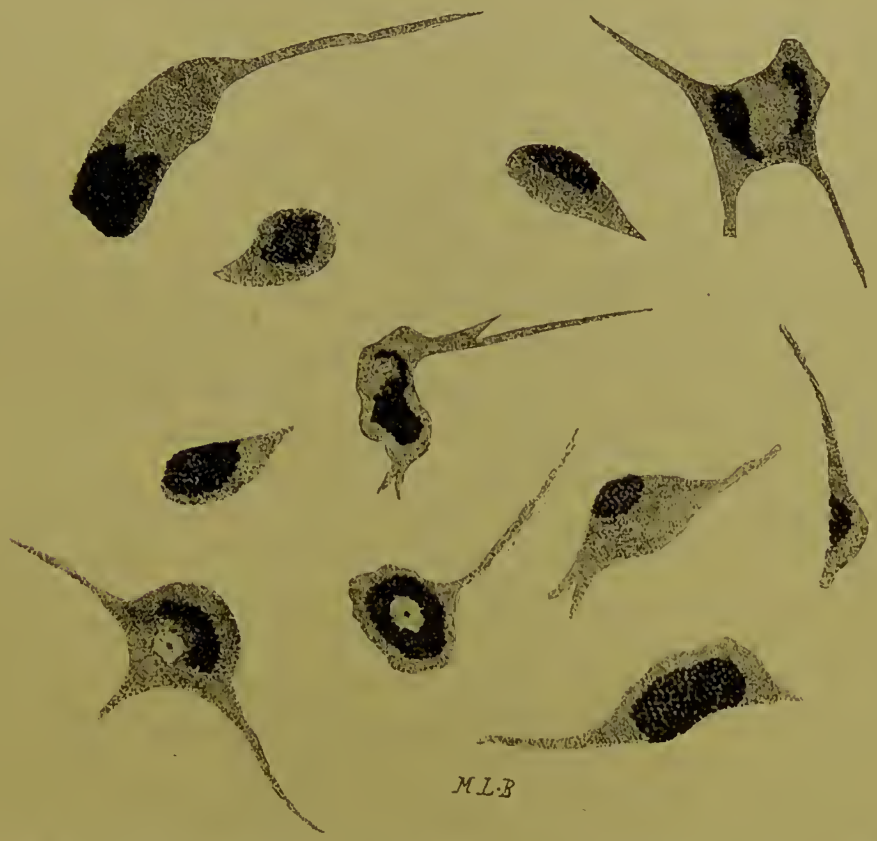


FIG. 9.—PIGMENT GRANULES IN NERVE CELLS. MARCHI'S FLUID. × 480.
Large multipolar cells of the ventral cornua of the spinal cord. The pigment is of a pale yellow colour when not subjected to the action of osmic acid.

As the result of tattooing, vermilion and Indian ink are found locally and may also occur in the nearest lymphatic glands. Argyriasis, a condition in which silver is deposited in the skin and causes a bluish-grey colouration, was formerly common when salts of silver were extensively given in the treatment of nervous diseases, but is rarely seen at the present day.

(11) LOCAL DEATH

During the progress of what we call 'Life,' cells and portions of tissue are continually being destroyed or dying, and being cast off. In the majority of cases their place is taken by new cells of exactly the same kind as those they replace, but in some instances the cells or portions of tissue disappear altogether, and in yet others they are replaced by a tissue of quite a different kind. Under pathological conditions, however, local death of another kind may occur.

Local death may concern large or small masses of tissue, but it is essential that a mass of tissue shall be involved; death of individual cells is never included under the term. Various names have been introduced in order to distinguish between different kinds of local death, and it will be convenient to describe separately (1) Gangrene, (2) Coagulative necrosis, (3) Colliquative necrosis, (4) Fat necrosis, and (5) Caseation. While describing these, the principal forms of local death, other terms will be explained.

(1) **Gangrene.**—Two forms of gangrene are known, dry gangrene or mummification, and moist gangrene or sphacelus.

The term **gangrene** is rarely used except in the case of a member or part of a member that has undergone local death. Gangrene of portions of the lung and gangrene of the entire pancreas are, however, known to occur, and gangrene of a portion of intestine or omentum is a frequent result of strangulated hernia. It is necessary in gangrene that the normal form of the dead part should be in a considerable degree preserved, so that the term is essentially a macroscopic one. Where the mass of tissue is small, and particularly when it is cast off, it is usually known as a **slough** if it consist of some soft tissue, or as a **sequestrum** if it be a portion of bone. When a portion of tissue has been killed outright by the action of some intensely powerful agent—e.g. heat or a strong acid—the dead tissue is termed an **eschar**.

Directly or indirectly, gangrene of all kinds depends upon an interference in the blood supply of the part in which the gangrene subsequently appears. This interference may be brought about in many ways, but fundamentally they all resolve themselves into obstruction of arteries or obstruction of veins. These two factors, indeed, practically determine the character of the gangrene that shall supervene; for if the arteries are obstructed, the gangrene is of the dry variety, whereas if the obstruction is situated in the veins, moist gangrene results. In either case, various causes may lead to the obstruction ; it may be that an embolus (Section VI) has lodged in the artery, or that its walls are so greatly narrowed by alteration of its coats that thrombosis takes place and completely obliterates the lumen ; it may be that some tumour compresses the vessels from the outside and causes a venous obstruction, or that an inflammatory process going on in the neighbourhood extends to the veins and leads to coagulation of the blood within them.

The differences that obtain between the two forms of gangrene depend upon just those different conditions that obstructions of arteries and obstructions of veins bring about. For it is clear that when the principal artery of a part is obstructed the part itself must be abnormally free from fluid, and that, on the other hand, when the veins are obstructed the exact converse must be the case. And since the fluid which is held in the part with obstructed veins is albuminous, and therefore an excellent medium for the growth of bacteria, it is clear that the chances of putrefaction are far greater in the case of moist than in that of dry gangrene. Moreover, the different amounts of blood held in the tissues in the two cases explain how those appearances which depend upon the disintegration of blood are very evident in moist gangrene, and inconspicuous in the case of dry gangrene.

In dry gangrene, therefore, the part becomes shrivelled and maintains its form, it becomes greyish purple or even black in colour, partly from the effects of drying and partly from modification of such blood as it contains ; it rarely becomes very offensive, owing to the relative absence of putrefactive changes ; and once these features have become established they undergo little alteration until the dead part is cast off (fig. 10). In moist gangrene, on the other hand, the part is swollen, the epidermis is apt to be raised in great blebs which hold a blood-stained serum, it is dark grey or black from the disintegration of the blood and its ultimate replacement by ferrous sulphide, and the odour given forth by the whole putrefying mass is intolerable.

Although the macroscopic appearances of a gangrenous part are unmistakeable, the microscopic changes are unsatisfactory. There is a general failure of the tissues to stain, or at most they take on an indefinite tint, with such a ground stain as eosin, nuclei are few or completely absent, and, though it may be possible to recognise some of the denser structures, such as bone, tendon, nerve, or artery, the more delicate structures have become fused in one mass of *débris*, in which oil-drops and crystals of ammonio-magnesium phosphate, and of fatty acids, are the sole distinguishable elements, if we omit mention of the innumerable bacteria of all kinds with which the mass teems.

Before leaving the subject of gangrene, a few additional points must be noted In the first place, it must be recognised that, although venous obstruction is the chief cause of moist gangrene, not every case in which there is venous obstruction is followed by this condition. For it is necessary that the obstruction should be complete, and, owing to the free anastomosis that obtains among the veins, this condition is not very often secured; it only occurs when all or the greater portion of a system of veins is affected, and hence it most commonly occurs when the part has been the seat of intense and extensive inflammation. Secondly, a part which is the seat of inflammation may become the seat of moist gangrene, but it can never become affected by the dry variety. Thirdly, it is not necessary that obstruction to the arteries leading to dry gangrene should depend upon an obvious cause. In the condition known as 'Raynaud's disease,' or 'symmetrical gangrene,' the obstruction which undoubtedly occurs in the arteries of such parts as the ears and fingers certainly does not depend upon any embolus or any pressure on the vessels from without, but as certainly does depend upon a spastic contraction, or some organic alteration, of the muscular coat of the arterioles. The same is true in the closely analogous case of 'ergotism,' in which localised foci of gangrene appear as the result of living on rye which is infected with *Claviceps purpurea* or *Ergot.* It has been experimentally proved that ergot causes marked contraction of the involuntary muscle of

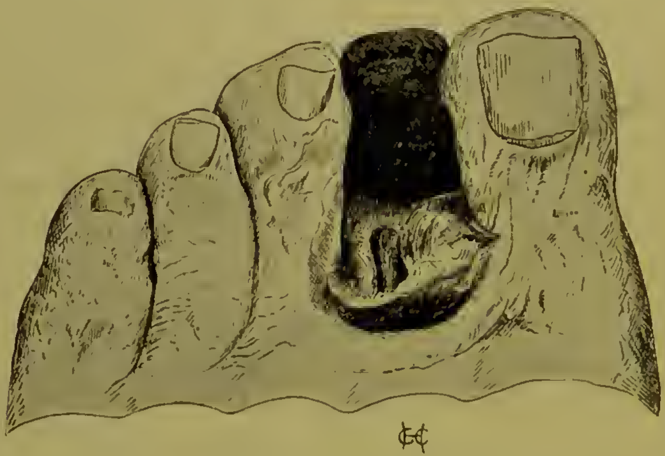


FIG. 10.—SENILE GANGRENE OF TOE. $\times \frac{3}{4}$.

The line of demarcation between the dead and the living tissue is well shown. At the base of the toe the extensor tendon is laid bare in the process of separation. The gangrene is of the dry variety.

small arteries. Fourthly, without going into the question as to whether there are, or are not, definite trophic nerves, there is no doubt that parts which have suffered a severe injury as regards their nerve supply, are more likely to become gangrenous than parts the nervous supply of which is normal. Acute bed-sores, in which a gangrenous condition appears over a large area within a very short time, are practically never seen except in persons who have suffered some extensive injury to the brain or cord. Lastly, adjuvant factors often assist the main cause in bringing about gangrene; the calcareous change in the small arteries, which is the prime factor in the production of senile gangrene, has a powerful adjuvant in the general feebleness of the heart-action which is usual in such cases.

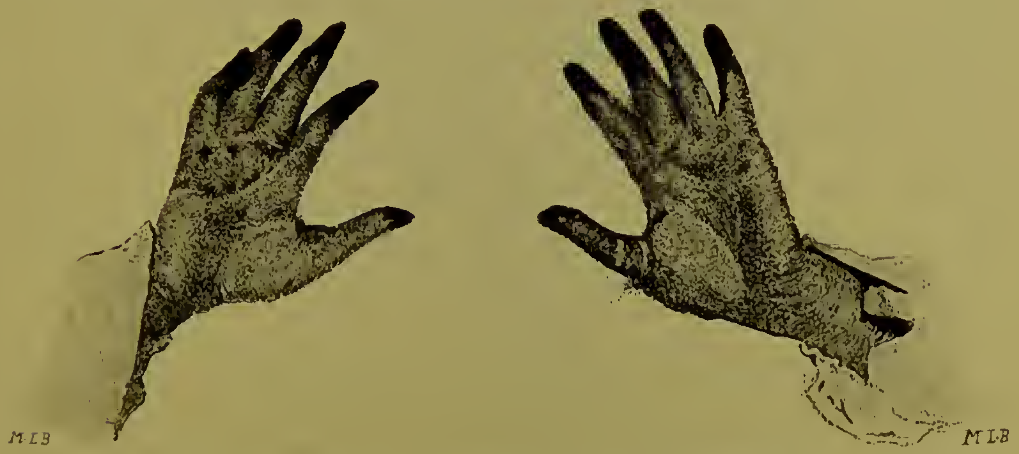


Fig. 11.—Hands from a Case of Raynaud's Disease. × $\frac{1}{6}$.
From a photograph in the Museum of St. George's Hospital. The extremities of the fingers and thumb on each hand are the seat of dry gangrene.

The manner in which a gangrenous part becomes separated from the living tissues in its immediate neighbourhood is one which practically consists in ulceration. The site at which separation is taking place is known as the *line of demarcation.*

(2) **Coagulative necrosis.**—This form of local death is of very common occurrence. It is met with wherever death overtakes a mass of cells that is infiltrated with an albuminous fluid, and therefore is especially likely to accompany all forms of inflammation of a more than ordinary degree of severity. Thus it is found in a typical form in the so-called 'false membranes' of diphtheria. Nevertheless, the existence of inflammation is not necessary for the occurrence of coagulative necrosis, for it is also seen in a simple infarct, where the whole process is aseptic and where inflammation, if it occurs, is a subsequent and subordinate phenomenon.

A mass of tissue which is the seat of coagulative necrosis is pale and anæmic, but it often shows at various points collections of extravasated blood. This anæmia is the effective cause of the local death, whether it is brought about by the pressure exerted on the capillaries by the inflammatory exudation (diphtheritic membrane), or whether it depends upon a definite obstruction to the supply of blood by the artery (anæmic infarct). The cells of which it is composed are swollen and granular, their nuclei stain badly, and often there is throughout the mass a delicate meshwork of fibrin. The mass stands above the ordinary level of the tissue in which it is placed, owing to the extra materials—fluid and fibrin—which it contains. Nevertheless, it is still in anatomical continuity with the surrounding tissues, and if torn away, rupture of the subjacent vessels leads to bleeding. It is probable that bacterial toxins play a considerable part in the production of the change.

(3) **Colliquative necrosis.**—This form of local death is never found except in the nervous system and particularly in the brain. It is closely bound up with the fatty change, and a part which has undergone colliquative necrosis always shows in it a great number of fat droplets. As the name implies, the dead tissue is in a fluid state.

(4) **Fat necrosis.**—This is a curious form of local death which affects fat in the abdominal area and especially the fat of the omentum. It is seen only when the pancreas is severely and extensively affected. Thus it has been met with when there has been hæmorrhage, abscess, or gangrene of the entire organ. When present, the areas of fat necrosis are seen as small dead-white, glistening masses, in the immediate neighbourhood of the pancreas. At times these masses are very numerous, at times not more than one or two foci, and these of very small size, are to be discovered. Occasionally groups of fatty acid crystals are present in the foci. It is fairly certain that the condition is the result of the action upon the fat of lipolytic ferment set free into the peritoneal cavity owing to the disorganisation of the pancreas. Experimentally, and in the very earliest stages of the change, the presence of a lipolytic ferment in portions of the omental fat has been demonstrated.

(5) **Caseation.**—Caseation is a form of local death which differs from those forms that we have hitherto described in respect of its chronicity. Gangrene and the other varieties are of sudden onset and run a rapid course, but caseation has more of the characteristics of the degenerations, in that its beginning

is insidious and its rate of progress far slower. Nevertheless, the amount of tissue that may become caseous is at times very extensive; the greater part of both lungs may be found in this condition after an illness that has not extended beyond a few weeks.

Caseation is a distinctly pathological change, it has no counterpart in normal life. It is, in essence, a fatty change, but it differs from ordinary fatty degeneration in many respects. Thus, it does not show itself in the form of droplets, it does not show itself under the same conditions or in the same tissues, and it tends to spread from a centre. At the same time, caseation has close relationship with coagulative necrosis. It differs from this change, however, both in its appearance and in the length of time that is necessary for its establishment.

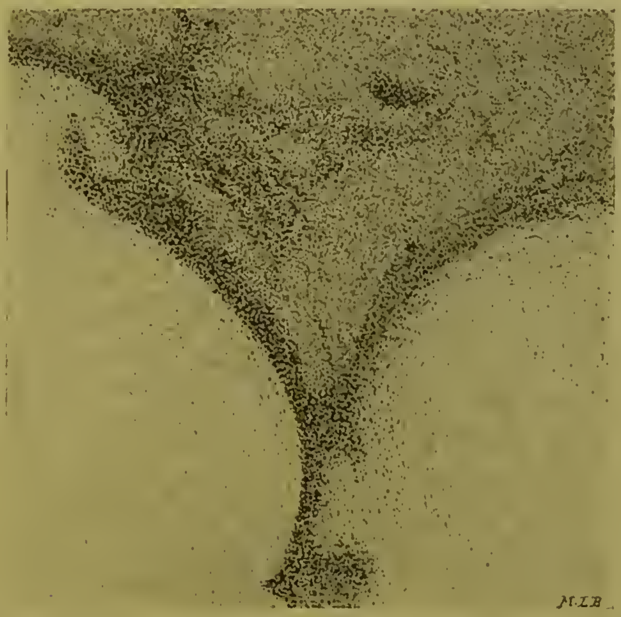


Fig. 12.—Central Caseation of a Tuberculous Mass. × 16.

Portion of a lymphatic gland showing the relatively unaltered lymphoid tissue (dark) with nuclei of many lymphocytes, and parts of two structureless caseous foci (light). The caseation is less advanced at the periphery of the foci.

A part that is the seat of caseation shows no trace of its former structure: cells, nuclei, blood-vessels, fibrous tissue, have all become merged into one indistinguishable mass of cheesy material which is quite structureless under the microscope, and simply presents the appearance of a poorly staining, finely granular mass (fig. 12). Here and there a number of irregular darkly staining granules may be visible, and these are minute foci of calcification, a change to which caseation is itself extremely prone.

Caseous material may remain in the body unchanged for an indefinite length of time, but this is not very common; as a rule it undergoes either calcification or softening. When it undergoes calcification the result is a mass of stony hardness, such as is often found in the bronchial glands; when it undergoes softening the ultimate result is a cavity in the tissue which represents the former situation of the caseous mass. For softening of caseous material is probably always the result of infection of the mass by bacteria, and a soft fluid or semi-fluid mass, in which there are bacteria, is to all intents an abscess, and, behaving like an abscess, 'points,' and tends to evacuate itself.

The chief situations in which caseation is found are themselves pathological. Thus it is particularly liable to occur in atheroma of arteries and in the chronic granulation tissue that is formed in tuberculosis and syphilis. Indeed, a gumma shows little more than a mass of cheesy material, and in the majority of tubercles the inflammatory material is only represented by a narrow ring around a large central caseous mass. Calcification of a caseous mass occurs far more commonly when the underlying condition has been tuberculosis than when it has been syphilis—in fact, we may almost say that the natural cure of tuberculosis shows itself in one form by the occurrence of calcification. Gummata, on the other hand, almost always soften, and the same is true in the, pathologically, closely allied condition of actinomycosis. The relative chances of the occurrence of calcification or of softening depend upon a variety of circumstances. The extent of tissue affected, the vitality of the patient, the seat of the disease, all have their influence, but it may, undoubtedly, be affirmed that, of the two sequels of caseation, calcification is, by far, the more favourable to the patient.

In certain situations caseous masses may form definite tumours. This is particularly the case in the cranial cavity, and then the caseous mass may often be shelled out of the bed in which it lies. Such caseous masses are more often tuberculous than syphilitic.

In the case of atheroma caseous changes are so common that recognition of atheroma is generally due to recognition of yellow caseous masses in the arteries, or else to the presence of the still further change of calcification. Probably the aorta is, of all regions in the body, the commonest seat of caseous change, for evidences of atheroma are present, in some degree, in the aorta of almost all persons above the age of forty. The subject of atheroma will be discussed more fully in the section upon the blood-vessels.

SECTION II

INFLAMMATION

It is probable that inflammation was one of the very earliest morbid processes that attracted the attention of the ancients from its general and widespread occurrence. Certainly the condition was known to Hippocrates (B.C. 430), and to Celsus (A.D. 32) we owe the recognition of the principal characteristics of the condition. For, under the name of 'cardinal signs,' he pointed out that **redness**, **swelling**, **heat**, and **pain** are present in almost all inflammatory states. To these four cardinal signs of Celsus a fifth, **impairment of function**, was added many centuries later; but since that time little has been added to our knowledge of inflammation from the macroscopic and the clinical points of view. The cardinal signs may be present in the most varying degrees in different cases, one or other of them may apparently be wanting altogether in a given case, they may in their combinations give rise to pictures of the utmost diversity, but nevertheless 'Rubor, Tumor, Calor, Dolor,' and 'Functio læsa' remain the most important phenomena of that protean state known as inflammation.

The macroscopic changes that are to be seen in inflammation vary very widely according to the part that is affected. Thus, when a loose and highly vascular tissue such as the lower eyelid is the seat of inflammation, there is an amount of swelling so great that it masks to a considerable extent the congestion that is undoubtedly present: when, on the other hand, the tissue is firm and resistent—e.g. the skin over the tibia—swelling is slight, but the redness is well-marked. In the case of a material like bone, in which the tissue is not only intensely resistent but is also relatively avascular, both redness and swelling are conspicuously absent. On the contrary, when the lung is inflamed, redness (at all events in the early stages) and swelling are most marked. Other differences in the characters of the inflammations are caused by the different degrees to which red and colourless blood corpuscles share in the process. Thus, the presence of an excessive number of red blood corpuscles causes the inflammation to be ‘hæmorrhagic,’ while if the leucocytes are present in excessive numbers the result is the formation of ‘pus,’ and the occurrence of a ‘suppurative’ inflammation.

A special subdivision of the inflammations is constituted by those cases in which the irritant is a micro-organism. Here we are liable to meet with the class of ‘spreading’ inflammations, and the explanation is found in the fact that the irritant is capable of multiplication and extension beyond the original focus at which it commenced to act. Another subdivision is made by the class of ‘specific’ inflammations in which the irritant itself is of a definite bacterial species, and the inflammatory products of its action have somewhat special characters.

Other terms applied to varieties of inflammation are ‘acute,’ ‘chronic,’ ‘subacute,’ ‘interstitial, ‘parenchymatous,’ but consideration of these will be deferred for the present, as they raise some very important questions.

CONGESTION

It has been said above that redness is one of the principal features of inflammation, but an excessive redness of a part may be present, and yet inflammation may be completely absent. The condition in which there is a great excess of blood in a part is known as **congestion** or **hyperæmia**, and it is clear that the causes of congestion may be many and various. Thus it may be due to the existence of an obstruction in the way of the venous return, and then we have ‘venous’ or ‘passive’ congestion. Or it may depend upon an alteration in vascularity on the arterial side, and then either there may be an active relaxation of the normal arterial tone, or the hyperæmia may be paralytic and dependent upon an injury to the vaso-motor nerves. Thirdly, both veins and arteries may be affected. From this it follows that we must distinguish between the forms of hyperæmia in theory, and the same is even more true in practice. Nevertheless, paralytic congestion is of far less common occurrence than the other varieties, and indeed is never seen except when some severe injury has involved the spinal cord or some of the main nerve-trunks of the limbs. Active, as distinguished from paralytic, congestion, and venous congestion, are, on the other hand, among the most common of morbid changes.

(*a*) **Venous congestion.**—Though venous congestion undoubtedly depends upon an obstruction to the return of the venous blood from the part, it must clearly be recognised that obstruction of a single vein, even though it be the main vein of the limb, is not sufficient to cause more than a passing congestion owing to the freedom of the venous anastomosis. It is only when the anastomotic branches are involved as well as the main stem that congestion of the distal parts occurs. For this reason the most marked cases of *general* venous congestion occur when the heart is at fault, and in particular when the right ventricle fails to contract with sufficient force to urge the blood it receives from the systemic veins through the lungs, and the most marked cases of *localised* venous congestion of the members when a tight ligature is placed around the part. In the latter instance it is necessary that the ligature should not be so tight as to completely obstruct the flow of blood through the artery; for under those circumstances the blood does not reach the part at all, and much less accumulates in the veins; if the circulation is thus cut off for more than a very short time, the part affected undergoes gangrene, which is a totally different condition.

A part which is the seat of venous congestion is swollen from the additional amount of blood which it holds, its superficial veins are turgid, and its colour varies from a purplish red to a deep purple according to the venosity of the blood within it, and therefore according to the degree to which its vessels are obstructed. If the cause of obstruction is not allowed to act for any length of time, upon its removal the part returns rapidly to its original condition, but if the obstruction acts for a very long time, and in particular if it is irremediable, the venous congestion becomes chronic, and is accompanied by certain changes involving the tissues of the part itself.

The principal change which occurs in a part the seat of chronic venous congestion consists in pressure atrophy, but other processes also occur, either concomitantly, or as a result of the pressure atrophy. In a liver which is the seat of chronic venous congestion, as the result of uncompensated heart disease, microscopic examination shows that the venules and the capillaries are engorged with blood, so that the distance between adjacent hepatic cells in a lobule is often considerable, instead of being, as is usually the case, almost inappreciable. At the same time there is often accumulated around the central venule of the lobule a quantity of light or dark brown granular pigment of hæmatogenous origin, and the bile capillaries become stained with yellow bile. The hepatic cells themselves are smaller than normal, of irregular size and shape, and are very frequently the seat of fatty changes, probably degenerative. As a result, light-coloured areas alternate irregularly with dark-coloured areas, and cause the macroscopic appearance of the liver to closely resemble that of a transverse section of a nutmeg. Here, then, we have pressure atrophy, pigmentation and fatty degeneration as results of chronic venous congestion. If the kidney derived from a similar case be microscopically examined, another result will be seen, viz. an increase of fibrous tissue in the part. For there is a general increase of the renal interstitial tissue which causes the organ to become very tough, and, by its contraction, gives it a granular surface and an adherent capsule. A good example of another morbid result of chronic venous congestion often occurs in the case of varicose veins. For, owing to the impaired nutrition of the skin over the dilated and congested veins, the pressure atrophy to which those veins give rise is sufficient to occasion the formation of an ulcer with deeply congested purple edges.

The occurrence of an increased formation of fibrous tissue is commonly said to be a usual result of long-continued venous congestion, and it is certainly present in many instances. But it is sometimes absent when it might be expected *a priori* to be present. Thus, it is not common for a great amount of fibrous tissue to be present in a 'nutmeg' liver, and though a spleen the seat of chronic venous congestion is extremely hard and is smaller than normal, it is not the seat of an excessive formation of fibrous tissue. And this, too, in spite of the fact that a kidney obtained from the same body, which had, during life, been subjected to the same degree of venous congestion, shows a well-marked fibrosis. Obviously, some other factor than the venous congestion alone is necessary for the production of the fibrosis, but what that factor is we do not at present know.

Next to cardiac disease as a cause of chronic venous congestion, the most important causes are various kinds of solid tumour. As a rule, the venous congestion in these instances is of the localised variety, involving, perhaps, one arm or one leg, but if the solid growth is situated in the thorax or in the abdomen, a more generalised venous congestion results. Though the actual nature of the solid growth which leads to a chronic venous congestion is, of course, of little importance in the special connection which we are considering, the rapidity with which it increases in size is of great importance. For if the tumour increases but slowly time is given for the establishment of a collateral circulation, whereas if it reaches a great size in a short time this is not the case. The same factor plays a considerable part in determining the extent of the venous congestion, for the more rapidly a growth is formed the greater the size which it is likely to attain, and *a fortiori* the greater the number of collateral vessels which it will obstruct.

The veins themselves in chronic venous congestion undergo certain changes, their walls becoming atrophied and thinned. Often, too, the lining endothelium suffers in its nutrition, with the result that venous thrombosis occurs. To these changes we shall refer when dealing with the pathological anatomy of the vascular apparatus.

(*b*) **Arterial congestion.**—This form of congestion, as has already been said, may be either of the active or of the paralytic variety. Active arterial congestion is a process of the commonest occurrence in normal life, for it is met with whenever a part is the seat of functional activity, but whether it occurs under pathological conditions is a different question. That it is met with in the neighbourhood of new formations that are rapidly growing, is true, but under these circumstances the change must be looked upon as physiological. It is when the congestion which accompanies inflammation is considered that an answer to the question becomes difficult. The subject is one that we cannot discuss here, but upon the whole it is probable that the congestion of inflammation is an active arterial congestion identical with that met with under physiological conditions.

Paralytic arterial congestion need not detain us for long, as it is of far less common occurrence than either of the two varieties of congestion we have already considered. It is usually very extensive, since it depends upon causes which involve large nerve trunks or even parts of the central nervous system itself. Thus, it is well marked in the abdominal area in cases of severe injury to the spinal cord at or above the seats of origin of the splanchnic nerves, and is the chief cause of the 'shock' which accompanies such cases. It occurs also when large nervous trunks carrying vaso-motor nerves are pressed upon by solid or other tumours. Thus, it is met with frequently when the large arteries of the thorax or the neck are the seat of aneurysm, when the lymphatic glands of the neck are the seat of secondary new-growth, and when the nervous trunks are themselves (e.g. exophthalmic goitre) the seat of organic change. In most instances of this kind the true paralytic congestion has been preceded by an arterial anæmia which depends upon a definite stimulation of vaso-constrictor nerves.

Whether the arterial congestion be active or paralytic, the part in which it occurs is redder than normal, and hot and swollen from the greater amount of arterial blood which it contains. At the same time, if superficial, it is often the seat of profuse sweating owing to the fact that the hidrotic nerves are also affected by the cause which leads to the dilatation of the arterioles. Paralytic congestion is not, however, accompanied at first by that increase of the lymph flow which is characteristic of active congestion. There is also a tendency for the arterioles, in cases of paralytic congestion, to regain their normal tone in some degree, owing to the independent activity of the local nervous mechanism in the walls of the vessels. In the case of both kinds of arterial congestion the dilatation of the arteries may be such that the blood in the veins is of arterial colour, the arterial pulse being also transmitted through the capillaries into the veins.

(*c*) **Hypostatic congestion.**—A variety of congestion is known which cannot be termed either arterial or venous, because both kinds of vessels (as well as the capillaries between them) are abnormally full of blood. By reason of their greater capacity and distensibility, however, the veins are the vessels which are most obviously the seat of change. This variety of congestion is of the greatest importance clinically, owing to the fact that it is dependent upon purely mechanical causes, and is very frequently the immediate precursor of death when the patient has been the subject of a long, exhausting illness.

Hypostatic congestion is the result of the action of gravity, and consequently is met with in dependent parts. It is quite independent of life; indeed the lividity which characterises the posterior aspect of a corpse which has been placed in the supine position after death is a typical example of hypostatic congestion. As a fact, life, meaning thereby continuance of the circulation, is antagonistic to the establishment of hypostatic congestion. It is therefore especially to be expected when the heart is failing (and particularly when the failure is due to the action of some poison, probably bacterial, upon the cardiac muscle and nervous apparatus) to keep up a normal circulation. It is easily intelligible that the lungs are the commonest seat for hypostatic congestion. For the right ventricle being the less muscular, and the blood-pressure in the pulmonary artery being low, any failure in the nutrition of the heart must show itself soonest in these parts. In fact, it is very rare to fail in finding evidences of hypostatic congestion of the lungs in any autopsy made on a case that has died of an acute disease of any duration.

A part which is the seat of hypostatic congestion is heavier than normal, of a deep red or purple colour, and when a section is made into it, dark blood drips from the cut surface in considerable quantity. Microscopically, the capillaries are wider than normal and filled with blood corpuscles, while as the result of the congestion a very considerable number of capillaries that are not normally obvious come into view. This is particularly the case with a tissue such as the pleura which, as viewed in a section of a normal lung, seems to be almost avascular (fig. 13). As a result of the central and local conditions, a part which is the seat of hypostatic congestion readily undergoes other changes. Hypostatic congestion of the lungs, for example, is soon replaced by a low form of inflammation, and passes into hypostatic pneumonia.

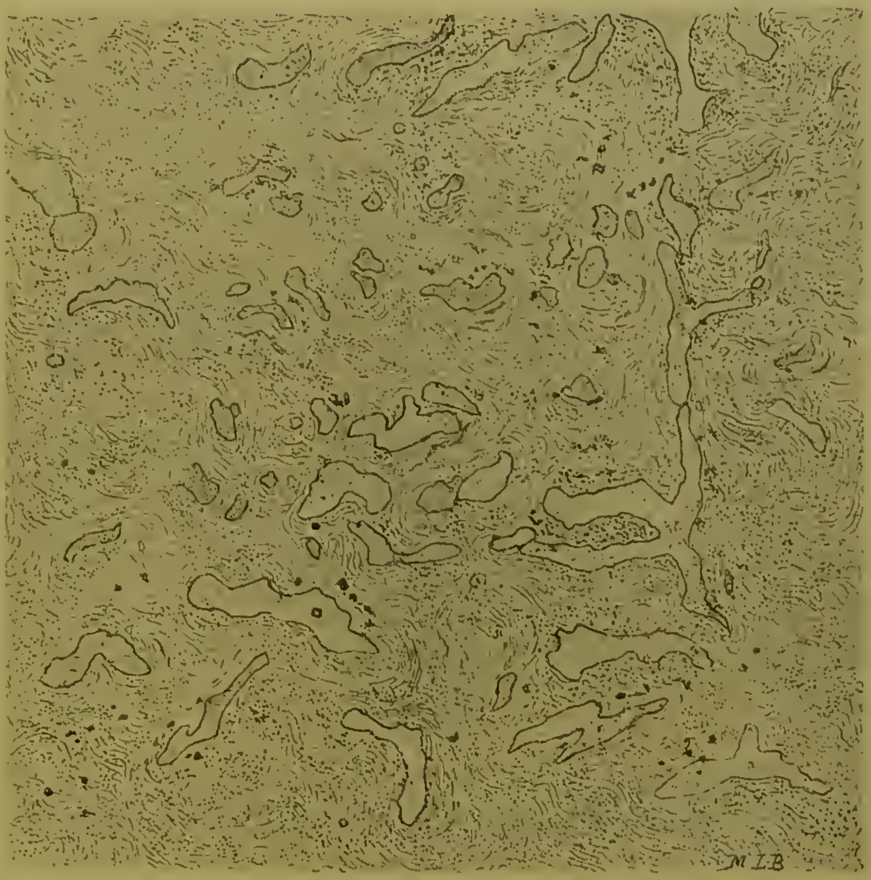


FIG. 13.—HYPOSTATIC CONGESTION OF THE PLEURA. × 60.
The section was cut parallel to the free surface, and shows the extensive capillary network in the pleura. The remaining portion of the tissue consists mainly of fibrous tissue.

ŒDEMA

The swelling which accompanies the establishment of inflammation in a part is in some measure the result of the increased amount of blood which is present in the vessels, but it is in very much greater degree the result of an accumulation of fluid between the actual elements of the part, and therefore outside the vessel-walls. The fluid that exudes from the small blood-vessels we know under the name of *lymph*, and it is clear that if for any reason the amount of lymph which is poured out exceeds the amount which is removed by way of the lymphatics and small veins, the excess must accumulate locally. There is no doubt that even in normal life the tissues vary considerably from time to time in the amount of lymph which they hold, but it is only when that increased amount of lymph is so great that it causes a noticeable increase in size of the part, that swelling or œdema is said to exist.

Œdema, then, consists in the existence of an excessive amount of extra-vascular fluid the characters of which more or less nearly resemble those of normal lymph. The fluid may be collected in different places, and its composition varies according to the situation in which it is found. At the same time special names are given to certain of the collections of fluid. Thus, œdema of the subcutaneous tissue is often known as **anasarca**, and the fluid itself is of low specific gravity (about 1008) ; when present in the serous cavities the condition is known as **ascites** (peritoneal cavity), or as **hydro-thorax** (pleural cavity), **hydro-pericardium, hydro-cephalus** (lateral ventricles), or, generally, as an ' effusion ' into the particular cavity concerned. When poured out into one of the serous cavities, the specific gravity of the fluid is somewhat higher than when poured out into the subcutaneous tissue (about 1016). When the effused fluid is definitely the result of inflammation it has a still higher specific gravity than those which have been mentioned above (about 1022), and, in addition, frequently differs in marked degree from the other kinds of œdematous fluid. The differences in the specific gravities of the different kinds of œdema fluid depend on the different amounts of proteid which they hold in solution, the total amounts of saline constituents, and the relative amounts of the individual saline constituents being remarkably constant, and differing but slightly from the amounts of these constituents in the blood plasma.

The conditions which lead to the occurrence of œdema are various, but the chief are venous or passive congestion, acute renal disease, and inflammation. The situations, too, in which the œdema fluid is poured out differ according to the cause upon which that œdema depends. Œdema, for example, which depends upon chronic heart disease affects principally the subcutaneous tissue of the lower limbs, with the great serous cavities as the disease approaches its termination; acute renal œdema, on the other hand, affects the subcutaneous tissue over the whole body irrespective of situation, excepting that it shows itself first of all, and to the greatest extent, wherever the tissue is loosest (e.g. the eyelids), and far less commonly involves the serous cavities. Inflammatory œdema, of course, appears wherever inflammation occurs, and its distribution is therefore quite irregular.

The amount of swelling that is present in inflammation varies within very wide limits, the chief causes of the variations being the density of the tissue in which the inflammation is taking place and the intensity and nature of the irritant. Thus there is the greatest difference between the amounts of swelling present in a case of inflammation of bone and in one of a loose tissue like the lung. So, too, the blister raised by the application of heat is evidence of a far greater amount of exudation than is that moderate swelling which accompanies the inflammation set up when cold has acted upon the part. But the importance of the intensity of the irritant in determining the amount of exudation is nowhere better seen than in the case of the bacterial irritants, for even in the case of one and the same species of micro-organism the type of the resulting inflammation may vary to so great an extent that it is almost impossible to believe that it depends upon merely a difference in intensity and not upon a difference in kind of the irritant. It is, however, possible by the adoption of certain means, which it is not necessary to specify here, to raise the virulence of a given species and prove the point conclusively. Speaking generally, it may be said that the amount of exudation poured out varies directly with the intensity of the irritant and with the looseness of the tissue upon which it acts.

Since œdema fluid approaches very nearly in its composition to the blood plasma, it is natural to expect that it should sometimes coagulate. But whereas blood plasma, if removed from the body, coagulates spontaneously after a longer or shorter interval, unless it be in certain exceptional cases, the same does not obtain so constantly with œdema fluid. In fact, the fluid of subcutaneous œdema does not tend to coagulate at all, either locally or after its removal from the body, though a coagulum readily forms on heating or on the addition of nitric acid. The fluid poured out in inflammation, on the other hand, readily coagulates *in situ*, and this fact explains, in large measure, the brawny swelling that surrounds a focus of acute inflammation. As will be seen when we come to consider the formation of pus, the coagulated material frequently undergoes a subsequent liquefaction. The tendency of exudations to coagulate is much greater when the fluid has been poured out into a serous cavity, whether the cause of that exudation has been inflammation, or acute renal disease, or heart disease. But the coagulation does not show itself by the clotting of the entire mass of fluid, but by the appearance in the cavity of smaller or larger masses of colourless fibrin. This fibrin may be loosely attached to the walls of the cavity, or may float free in the fluid; in the former instance it is often said to have formed a 'false membrane' on the wall of the cavity. Unfortunately, the name 'lymph' has been given to the solid fibrin separated from exudation fluid; it is still frequently used, but, since the name has been long applied in physiology to a liquid of known characteristics, and since the solid material separated from exudation fluid is nothing else than fibrin, this term is greatly preferable to that of lymph.

The exudation fluid in inflammation frequently contains other solid materials than fibrin. It almost invariably contains a certain number of leucocytes, and that number may vary between the widest limits. Thus it is at times very difficult to find a single leucocyte in a case of acute peritonitis, and, on the other hand, these cells may be present in numbers so considerable that they give to the exudation a creamy appearance and consistency. Red blood corpuscles, too, may be present, and may be so few that they are recognisable only by means of the microscope, or so numerous that the fluid has the appearance of rather watery blood. When the inflammation has been due to the action of some bacterial irritant, the exudation fluid may also contain varying numbers of micro-organisms, and the same is true if bacteria of putrefaction have gained access to the fluid after its formation.

It will be necessary to refer again to the exudation when we are considering the types of inflammation and the formation of pus.

INCREASE OF TEMPERATURE

It is a matter of common knowledge that a focus of inflammation in the superficial parts is hotter than the surrounding tissue. Formerly it was thought that the rise of temperature might cause the focus of inflammation to be hotter than the rest of the body, but it is now known that this is not the case. The local temperature only approximates more closely than the surrounding parts to the temperature in the internal portions of the body. The increased heat is due to the local dilatation of the blood-vessels which allows of a more frequent renewal of blood, and permits a given sample to remain in the superficial part and there lose heat, for a shorter period of time. When it was considered that the temperature of an inflamed part may be greater than the rest of the body, this apparent 'fact' was held to be dependent upon the setting free of heat as the result of the chemical processes going on at the focus of inflammation. And though it is of course clear that any heat that may be locally formed must be rapidly distributed over the whole body by means of the circulation, it must not be concluded that chemical changes accompanied by a formation of heat do not occur locally because the conclusion as to the local temperature has been proved to be wrong. On the contrary, it is in the highest degree probable that there is a local formation of heat in inflammation, though the heat so formed goes to warm the whole mass of blood as it is produced.

PAIN

The pain in inflammation varies considerably in intensity, and is largely due, no doubt, to the stretching of the delicate nerve fibrils brought about by the dilatation of the blood-vessels, and to the pressure to which they are subjected owing to the exudation which takes place into the extra-vascular lymphatic spaces. The last-mentioned cause is of the greatest importance in determining the amount of pain, as can be readily recognised by considering the difference between the pain experienced when the tissue in which the inflammation is taking place is dense and resistent on the one hand, and when it is loose and relatively non-resistent on the other. Thus, the pain which accompanies the formation of a small abscess at the root of a tooth far exceeds that of an abscess of the same size formed on the dorsum of the hand, while it is a matter of common experience that a pustule on the septum of the nose is far more painful than one on the ala.

But while there is no doubt that the pressure to which the nerve fibrils are subjected plays the most important part in determining the amount of pain, it is also possible that other factors contribute in producing the final result. Thus it is possible that the nerve endings are directly stimulated by some of the chemical substances which are undoubtedly formed at the seat of inflammation.

IMPAIRMENT OF FUNCTION

In many instances it is unnecessary to do more than mention the fact that when a part is inflamed its function becomes disordered. This is particularly the case when the function of the part is movement; the interference with the muscles of mastication that accompanies any inflammation going on in their neighbourhood, and the impairment of locomotion which accompanies the presence of any focus of inflammation about the muscles or joints of the lower limb, are too well recognised to call for special remark. The causes of these interferences in the exercise of function are the swelling and the pain, so that the impairment of function is partly mechanical and partly voluntary. But these considerations do not constitute the whole explanation. For if a microscopical examination of a portion of the muscle in the immediate neighbourhood of the focus of inflammation be made, it will be seen that the muscle fibres have themselves undergone change. They will be found to have lost, in less or greater measure, their striation, and may be swollen and granular or even broken up into portions. At the same time the intermuscular fibrous tissue appears to be more extensive than normal, because of the increased amount of fluid which it holds between its meshes, and also is infiltrated with a number of small round cells. Thus, not only is the essential contractile material itself the subject of profound change, but also such fibres as may have escaped act at a disadvantage owing to the alteration in form and stability of the solid substructure against which the muscular elements normally contract.

In the case of other tissues and organs the statement that impairment of function accompanies inflammation is no less true, though it is at times not so obvious. When the lung is inflamed the amount of exudation poured out is so great that it penetrates into the alveolar air spaces and displaces the air. As a result, the portion of lung so affected becomes useless for purposes of respiration, and the impairment of function is to be recognised, not directly, but by the increased function exhibited by the still unaffected portions of lung in their endeavour to compensate for the local loss of function. Thus in pneumonia, where a considerable portion of the lung is, as a result of the inflammation, rendered temporarily useless, the respirations are quickened and not slowed in rate. It is true that at the same time the individual respirations are commonly shallower than normal, but nevertheless the increase in rate more than counterbalances the diminution in depth of the individual respirations, and the total respiratory exchange is increased.

In the case of the kidney, the effect of inflammation upon function is usually to be seen directly in a diminution in the amount of the urine secreted; indeed in very severe cases secretion of urine may fail altogether. But the impairment of function is also recognisable in the more or less profound alteration of the urine itself. Owing to the disorganisation of the renal epithelium the passage of the albumin of the blood plasma into the urine is no longer prevented, and it makes its appearance in the urine, often together with numbers of red and white blood corpuscles. At the same time the excretion of urea and the other nitrogenous metabolites of the body is interfered with, and the amounts of them present in the urine is less than normal.

In the case of other glands the effect of inflammation in impairing function is often not at all obvious, for a variety of reasons. The liver, for example, though it is the largest gland in the body, is comparatively seldom the seat of ordinary inflammation, and even when it is, the entire organ is not affected, so that complete arrest of function is never seen, and as a rule disorganisation of function is not recognisable. This is partly due to the size of the organ, partly to its multiplicity of function, and partly to the difficulty there is in the way of experimental work upon it. It is impossible to doubt, however, when one considers the extreme disorganisation often seen under the microscope, that a correspondingly great impairment, or even a complete abrogation, of function has occurred at the sites of inflammation.

In many instances impairment or abrogation of function results, as a consequence of the anatomical changes which inflammation brings in its train. Thus, a testis which has been the seat of acute orchitis may become so gravely modified by subsequent change, that it becomes functionless, although it still preserves its gross anatomical features. The microscope, however, scarcely ever fails to reveal the condition upon which the loss of function depends. To changes of this description we shall return later.

CELLULAR CHANGES IN INFLAMMATION

The cellular changes in inflammation constitute some of its most important phenomena. From what has already been said it is clear that the vascular system and the blood play fundamental parts in the process, and it might be supposed that since red corpuscles form the most numerous element in the blood, they should also play the most important part in inflammation. This is, however, far from being the case; in fact, they appear to play nothing more than a passive part throughout, while the leucocytes which are present in the blood in relatively small numbers take, in inflammation, a position of fundamental importance.

The tissue cells, and in particular the connective-tissue cells, also play an important part. But whereas the greatest activity of the leucocyte seems to be shown during the actual progress of the inflammation, the greatest activity of the connective-tissue cell seems to be shown after the inflammation has subsided. Not, indeed, that it can be said that the connective-tissue cell is inactive during the actual progress of the inflammation, for, as will be seen later, there is the strongest reason for believing that the tissue cells (i.e. the connective-tissue cells) exercise very important functions of a kind similar to those exercised by the leucocytes.

The microscopic changes in inflammation may be best studied in the frog, and it has been conclusively proved that they are in essence the same in cold- and in warm-blooded animals. If a frog be pithed, or better if it be curarised, and a coil of intestine be drawn through a laterally placed opening in the abdomen, and the attached mesentery be examined with a low power of the microscope (care being taken that the mesentery does not dry), a series of changes will be noticed. At first there is a constriction of the blood-vessels, but this is seldom seen, as it is of very short duration. To this there follows a dilatation which primarily concerns the arterioles, but which soon involves the venules by reason of the greater quantity of blood which they are called upon to carry away. At the same time the capillaries are noticed to be fuller of blood than normal, and many capillaries which were not previously seen come into view. On the first establishment of this dilatation of vessels the blood is seen to be coursing along with greatly increased velocity, so that the form of individual corpuscles can no longer be recognised, and there no longer remains a distinction of the blood stream into axial and plasmatic layers. But soon the velocity diminishes, though the blood-vessels still remain dilated.

This slackening of the blood stream with continued dilatation of the blood-vessels marks a very important stage in the inflammatory process, for it is now that the cellular changes begin to manifest themselves. Under ordinary circumstances when the blood stream can be distinguished as consisting of an axial and a plasmatic layer, the blood corpuscles, red and white, travel in the axial stream. Now and then, owing to its inferior specific gravity, a leucocyte passes into the plasmatic layer, but it does not commonly remain there long, and is soon swept again into the axial layer. But when the vessels are modified in the way we are considering, the appearance of the plasmatic layer (so long as a plasmatic layer is visible) is very different. For the leucocytes tend to collect in the neighbourhood of the vessel-wall, and often form small accumulations which are quite unlike anything seen in a normal vessel.

While the above facts are being recognised, it will probably be noticed that one of the small vessels—probably a capillary or a small vein—shows a small prominence on its outer side which gradually increases in size, and ultimately becomes separated from the vessel-wall. On careful examination it will be found that this excrescence from the outer surface of the wall of the vessel takes place at the expense of a leucocyte which was attached to the inner surface, and in a fortunate instance the whole process may be watched. The leucocyte definitely passes through the vessel-wall, and in the middle of the process the two knobs of protoplasm on either side of the wall are connected by a thin strand which traverses the entire thickness of the wall. The process is known as 'migration.' It is uncertain whether the process is an active or a passive one.

Concerning the part played by the red corpuscles in inflammation there is no doubt. It is on all sides agreed that the extrusion of these cells, which is a very common phenomenon, is a purely passive process. They are bodily thrust through lacerations in the vessel-wall, remain at the spots at which they have been extravasated, and only travel thence in so far as they are passively carried away by the lymph. Neither do they fulfil any of those functions which we shall see are carried out by the leucocytes, but their further history is one of degeneration and removal.

CHEMIOTAXIS

By this name a phenomenon is designated which appears to play a very important part in inflammation and in the closely allied subject of immunity. It was found that certain of the plasmodial members of the lower vegetables which possess the power of amœboid movement have the direction of that movement modified according to the nature of the substances in their neighbourhood, Further, it was found possible to determine the direction that the plasmodium should take on a wet surface along which it could travel, by presenting to it one or other of a series of chemical substances. As a result of these experiments the substances were divided into two great classes according as the plasmodium travelled towards the chemical substance or in an opposite direction. When the plasmodium travelled towards the chemical substance the latter was said to exert a 'positive chemiotactic' influence upon the plasmodium and 'positive chemiotaxis' was said to occur. When the chemical substance caused the plasmodium to move away from it, the condition was called 'negative chemiotaxis.' Experiments were then made upon the subject in the living animal body, and it was found that a phenomenon similar to positive chemiotaxis undoubtedly occurs, the leucocytes taking the place of the plasmodium. With regard to negative chemiotaxis, the matter is not so clear. It is not certain that an actual repulsion of leucocytes ever takes place, though it is allowed by those authorities who cannot accept the belief that negative chemiotaxis occurs in the animal body, that it is not infrequent to notice a failure of attraction of leucocytes. Regarded as bearing this modified interpretation, the term 'negative chemiotaxis' is of undoubted value.

Positive chemiotaxis is a far commoner phenomenon than its opposite, and since, as we shall see later, the vast majority of inflammatory manifestations depend upon the action of a bacterial irritant, it is important to note that, of all varieties of chemical substance, none have been found more potent than the bacterial products in leading to a local accumulation of leucocytes, i.e. in producing positive chemiotaxis. The best example of a substance which leads to negative chemiotaxis is afforded by quinine.

PHAGOCYTOSIS

When a collection of leucocytes has taken place around a focus of irritation, another phenomenon manifests itself. Certain of the leucocytes are seen to hold foreign substances within their bodies. The process whereby the leucocytes take up these particles and the subsequent fate of the particles themselves constitute the series of changes known as **phagocytosis**.

In a great many, if not in all, points of its life-history, the leucocyte bears a strong resemblance to the amœba, and in particular the method in which they ingest particles is identical. The process consists in the thrusting out of pseudopodia and encircling the particle. When the particle has been entirely surrounded by the protoplasm a vacuole is formed around it. In this vacuole the particle is digested if it be digestible, but if it is indigestible it is held for a shorter or longer time, and is then simply extruded from the body by a process exactly the reverse of that by means of which it was incorporated. In the amœba this function is certainly subservient to nutrition, but in the leucocyte the matter is not so clear. *A priori* one would expect that the leucocyte should derive its nourishment from the blood plasma or the lymph in which it is circulating rather than from the solid particles which it meets, so to speak, accidentally. The amœba, however, undoubtedly takes up at times particles which it does not digest, and it is certain that the leucocyte will take up materials (e.g. carmine particles) which are utterly useless from a nutritive point of view. It is therefore generally held that whatever the original object of the function may have been, in the case of the leucocyte it is no longer nutritive but rather of a 'scavenging' character. Metchnikoff, however, to whose researches upon the subject we owe the greater part of our knowledge, holds that leucocytes are more than mere scavengers. He considers that they are directly concerned with the defence of the animal in which they are present from bacterial attack, that they are the chief factors in determining whether he shall become infected or shall remain immune, and that, if they are not entirely able to resist the invasion, they play a very important part in determining the type of the illness which results.

Whatever may be the true explanation of phagocytosis, and it may be here said that the majority of modern authors incline towards the 'scavenging' view, there is no doubt that when an accumulation of leucocytes has followed the entry of some bacterial irritant into the body, we often find numbers of leucocytes holding bacteria in their interior. These bacteria sometimes stain well with the ordinary aniline dyes, but sometimes they afford distinct evidence that they are in some measure degenerated. Sometimes, too, they are contained within a vacuole, and then there can be no doubt that phagocytosis has taken place, but they may not be surrounded by a vacuole, and then it is very difficult to decide whether they are contained within the actual body of the leucocyte or whether they are merely adherent to it.

But it is necessary to look into the matter of phagocytosis a little more closely. We know that all leucocytes are not of the same kind, but that we have to distinguish between those which are provided with granules and those which are destitute of them. Moreover, in mammals, two kinds of granular leucocyte are met with in the blood and lymph, namely, one having a large number of coarse granules which stain with acid dyes (eosin, &c.) and a large horseshoe-shaped nucleus, and forming about 2 to 5 per cent. of the leucocytes of the blood, and the other having a multilobed nucleus and a number of very fine granules which stain with acid dyes. The last-mentioned variety of leucocyte shows many differences in different mammals, especially as regards the avidity with which the granules take up the stain ; they agree, however, in forming about 60 to 70 per cent. of the leucocytes in the blood.

Of these granular leucocytes the cells with coarse granules are non-phagocytic, but the cells with fine granules are, on the contrary, intensely phagocytic. Phagocytosis is also a property of the large non-granular cell with a large, round or oval, poorly staining, nucleus which is present in the blood, and is known as the *hyaline* or the *mononuclear* cell.

Phagocytosis is not a function of hæmal leucocytes alone, however. Numerous other varieties of cell possess the property. Thus it is exercised by the endothelial cells lining the capillaries of the liver, by certain varieties, at all events, of giant cell, and it is probable by a large number of tissue cells, in particular by young and rapidly proliferating connective-tissue cells. With regard to the last-mentioned variety of cell, however, we are not able to speak with absolute certainty, though the probability that it is phagocytic is very great.

PUS

It will be convenient here to consider the characters of pus. The conditions under which it is formed will be considered along with the question of abscess formation (p. 68).

Pus, in the form in which it is most commonly seen by the surgeon, is a fluid of creamy appearance and consistency, having a specific gravity of 1030–1033. It is usually not auto-coagulable and, on standing, separates into a thick opaque deposit and a clear supernatant fluid. It has an alkaline reaction and a faint mawkish smell. A characteristic reaction is that on the addition of a solution of a caustic alkali, the pus becomes 'ropy.' This is due to the fact that it contains a considerable amount of either mucus or nucleo-proteid, or both.

When a drop of pus is examined under the microscope, it is seen that it consists of a large number of colourless cells with definite nuclei and granular protoplasm. This is the usual appearance, and the invariable one if the pus has been derived from an acute abscess. But if the pus has been obtained from a chronic, or as it is sometimes called a *cold,* abscess, it may be impossible to find a single cell. The pus has all the appearances of pus from an acute abscess, it throws down a copious creamy deposit on standing, but this deposit does not consist of cells as in the other instance, but of a granular amorphous material containing fat globules.

If a drop of dilute acetic acid be run in under the coverslip while the pus cells are kept under observation, it will be seen that the granular contents of the cells become cleared up, and the nuclei are seen much more distinctly. It is obvious, since the granules clear up in dilute acetic acid, that they are not fat; is nevertheless, that they are probably on the way to become fat is shown by the facts that fatty degeneration of pus cells is common, and that so large a quantity of fat is present in the pus from a cold abscess. In a large number of instances the character of the granules can be made out by staining. This is particularly the case with pus that is of very acute formation; on staining a film of gonorrhœal pus, for example, with eosin and methylene blue, the granules of the pus cells take on a brilliant red colour, and the cells themselves bear the closest resemblance to the finely granular leucocytes of the blood (Plate VI.)

Sometimes a pus cell has a single nucleus, but this is not usually the case. Usually two or more nuclei are present, and, indeed, the multiplicity of the nuclei of pus cells constitutes one of their principal characteristics. Though the presence of more than one nucleus in a cell is generally a sign of proliferation, it must not be so regarded in this instance; on the contrary, it is probable that it is a sign of degeneration.

Though the cells which have been described above are those most commonly met with in pus, a varying number of cells, with an entire absence of granules, is also met with. Red blood corpuscles are often present, and sometimes in numbers so considerable as to give a bloody appearance to the pus; but they are to be regarded as accidental constituents.

For a long time the question as to the origin of pus cells provoked the most animated discussion. Some authors held that they are derived from the tissue cells (Stricker), and others that they are nothing more than migrated hæmal leucocytes which have undergone some slight degeneration (Cohnheim). There is no doubt that the latter view is the more nearly correct; we can see the leucocytes migrating through the vessel-wall, and we find that pus cells may correspond even to the manifestation of amœboid movement, when placed on the warm stage, with the migrating cells. But we have now receded from the too dogmatic opinion of twenty years ago, and recognise that a portion of the pus cells is derived from the tissue cells. It is to the non-granular cells in pus that we are inclined to attribute this origin.

The fluid portion of pus—*liquor puris*—is not mere *liquor sanguinis*. We have seen that one of the principal changes which supervene on the action of an irritant upon a vascular part is a more or less considerable exudation of fluid through the walls of the capillaries and small veins. This exudation fluid no doubt constitutes the foundation of the liquid portion of pus, but there are added to it numerous substances derived from other sources than the blood. The lack of auto-coagulability of pus is but one intimation of the differences between the two fluids, and along with this lack of auto-coagulability there goes the presence in pus of certain elements that are wanting in blood plasma.

The fluid which exudes from the blood-vessels in inflammation shares in the characters of ordinary blood plasma so far as coagulability is concerned; in fact, inflammatory blood, and, *pari passu*, inflammatory exudation fluid are excessively prone to coagulation. And when poured out into the tissues the exudation frequently coagulates, and leads to certain particular forms of inflammation. But even a coagulable fluid does not coagulate except under certain circumstances, amongst which the addition to the fluid of a small quantity of some tissue proteid is one of the most important. Now in inflammation we not only have a coagulable fluid present in the extra-vascular spaces, but also the irritant action which has led to the exudation from the blood-vessels has destroyed or severely injured a number of the tissue elements in the neighbourhood of the vessels which are giving exit to the exudation. Coagulation, therefore, takes place about the seat of irritation, but, as a rule,. it is not of long duration. For in a very large number of cases the cause of the inflammation—the irritant—is a variety of micro-organism, which produces as one of the results of its life-history a proteolytic enzyme, which acts upon the coagulum and the dead tissue elements entangled with it, and dissolves them. It is clear, therefore, that we must not expect pus to be auto-coagulable, and that we must expect it to contain the ordinary products of proteolytic action, together with any substances which may be special products of the irritant itself. We therefore find albumoses in pus, together with leucin, tyrosin, and varying amounts of the later products of fatty degeneration.

In close connection with inflammation come a number of changes involving the fixed tissue cells. These changes are of two kinds, degenerative and proliferative, and by many authors they are considered equally as being included under the conception of inflammation. With regard to the degenerative changes there is no doubt, for inflammation is the series of changes which follows upon the action of an irritant, and we can easily conceive that an irritant should lead to degeneration. But with regard to the proliferative changes the matter is different, for proliferation is a manifestation of growth and is called into existence by a stimulus. It is true that at some point or other every irritant must cease to be an irritant and must become a stimulus. Hence, though we cannot but admit that the proliferative changes in the tissue cells are closely bound up with the degenerative changes of inflammation, in so far that proliferation must, *cæteris paribus*, follow immediately upon the degenerative changes, we are forced to separate them sharply, confining the degenerative changes in the tissue cells to inflammation, and relegating the proliferative changes to *repair*, one of the most important of the *sequels* of inflammation.

THE CAUSES OF INFLAMMATION

Though a fully satisfactory definition of inflammation has never yet been given, it is agreed that for its production the action of an irritant is necessary. Irritants are of the most diverse nature. They may be mechanical, such as a muscular strain, chemical (acids, alkalies, &c.), physical (light, heat, cold, electricity), or they may be living (animal or vegetable). Broadly they may be divided into two great classes according as they are living or non-living. Of these two classes the living is by far the more important, partly because the action of living irritants almost invariably complicates the action of an otherwise non-living irritant, and partly because, as a very result of its life, a living irritant is capable of a far more extensive action than a non-living irritant. It may also be said, indeed, that the importance of a non-living irritant as an inducer of inflammation depends upon the fact that it opens the way for the action of a living irritant. Were it not for the living irritants, inflammation, as we know it, would be extremely rare.

The variety that obtains amongst the non-living irritants is so considerable that no good purpose would be served by considering them further here, but the case is different with the living irritants.

Living irritants are either animal or vegetable. Of these two classes vegetable irritants are the more important, for they include the whole group of the Schizomycetes. This group is often spoken of, collectively, as the bacteria, and in it are contained several different species, the most important of which are the **bacilli**, the **micrococci**, and the **spirilla**. All of these species belong to the order of fungi, but the *true* fungi or moulds, which are botanically closely allied, are seldom the causes of inflammation. As their name implies, the bacilli are rod-like in shape, and this characteristic they maintain however much they may vary in size or shape, in the ratio that obtains between their length and their breadth, or in their other characteristics. They multiply by fission, and the rate of their growth is such that under suitable conditions they double in number in twenty minutes. Certain of the bacilli also possess a special mode of reproduction. They produce in their substance small oval or round highly refractile bodies called *spores*. These spores are extremely resistent to many agencies which readily destroy the bacilli themselves, e.g. heat, cold, chemical substances. They also appear to preserve their power

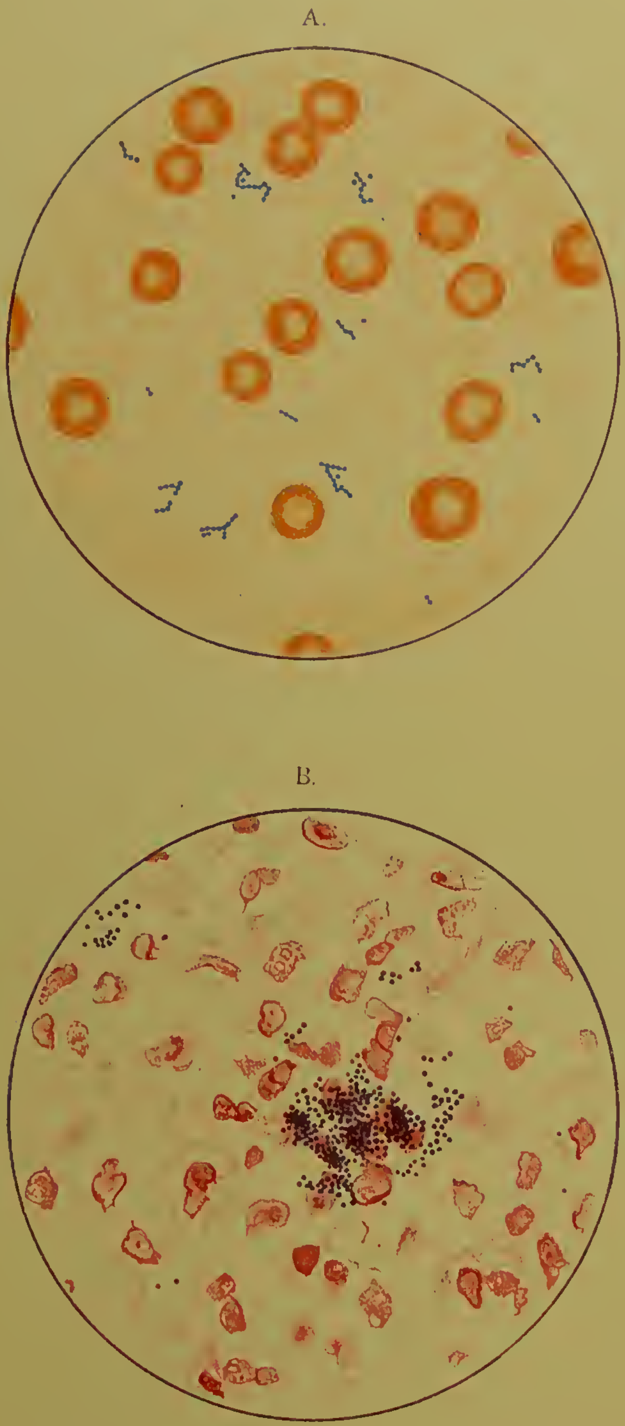
PLATE III

Fig. A. Coverslip film of blood showing streptococci. From a case of puerperal septicæmia. The blood was taken from the median basilic vein during life, was inoculated into beef-broth, and incubated 24 hours at 37° C. No bacteria could be found in the blood itself by the coverslip method. The micro-organism is streptococcus pyogenes. Film fixed by heat, stained by watery eosin and watery methylene blue, and mounted in Canada balsam. Magnification about 800 diameters.

Fig. B.—Section of liver, showing a small pyæmic abscess and a central mass of staphylococcus pyogenes aureus. No actual liver cells are seen in the section, the nuclei visible being those of pus cells. Owing to the method of staining, the micrococci appear larger than the streptococci in fig. A, but are in reality of about the same size. Tissue hardened in alcohol, embedded in paraffin, stained with alum-carmine, and subsequently, by Gram's method, mounted in Canada balsam. Magnification about 800 diameters.

Note.—These figures illustrate the difference between septicæmia, in which the micro-organisms multiply in the blood, and pyæmia, in which the micro-organisms are carried by the blood, but multiply in the tissues, where they become lodged, and there lead to the formation of abscesses.

Plate III.



Micro-Organisms in Blood and in Pyæmic Abscess.

of germinating, when placed under suitable conditions, for an indefinite length of time. It can easily be recognised that the question whether a given bacillus forms spores or not has a most important bearing upon the methods to be adopted when dealing with it.

The micrococci are spherical organisms and are divided into different varieties according to their mode of multiplication. Thus, amongst the **streptococci** (Plates IV, A and V, A) multiplication takes place in one direction only, with the result that the micro-organism forms longer or shorter chains; among the **staphylococci** (Plate IV, B) multiplication takes place in all directions, with the result that 'heaps' of cocci are formed. The greater number of micrococci divide after one or other of these two fashions, but varieties are known in which the cocci are found joined together in pairs (Plate V, B), each pair being surrounded by a translucent capsule (**diplococci**), or in which division takes place in two planes, with the production of masses that look like bales of wool tied up with a cord that divides each surface into four equal parts (**sarcinæ**). It is uncertain whether spore-formation takes place among the micrococci, but if it does, it is very uncommon, and is different from the process that occurs among the bacilli.

Spirilla are organisms of which the characteristic shape is a spiral. The number of turns in the spiral varies between wide limits; often it is ten or more. Sometimes, however, the entire organism is only represented by a portion of a spiral; under these circumstances it is called a **vibrio**. So far as is known, all members of this group are motile, a property which also belongs to certain of the bacilli, but which is not met with among the micrococci, with one or two exceptions.

Theoretically all varieties of micro-organisms may act as irritants, but as a matter of fact it is only a small number that are concerned with the production of disease. These—the *pathogenetic* bacteria—have been distinguished from the non-pathogenetic bacteria, and are the only ones that are of interest from our present point of view. All the pathogenetic bacteria produce disease by acting as irritants; in other words, by leading to inflammation. It is true that in some cases the variety of inflammation produced has very special characters, so that we are able to state with approximate certainty, from an examination of the gross and microscopic appearance of the disease, the nature of the micro-organism which has caused it. But it cannot be too soon or too clearly stated that, in the consideration of disease, inflammation, in one or other of its numerous forms, plays a more important part than perhaps any other pathological process. In particular, it lies at the bottom of all the morbid conditions which depend upon the activity of bacteria, however little that may appear to be the case at the first glance.

The bacteria act as irritants, in part, by their very presence; in that degree they may be likened to the mechanical irritants, though their power of multiplication has also to be taken into consideration. But they bring a much more important factor into play which differentiates them from all other varieties of irritant. For it is a characteristic of the bacteria that they produce, as the result of their life-history, various substances in the medium in which they are growing. These substances, which are commonly included under the name of 'toxins,' are apparently of very different kinds. Many of them are intensely poisonous, and it is these which have given the name to the whole class; but some possess the power of peptonising proteids, others of splitting up sugars and other chemical substances, and so on. The actual nature of the toxins is at present a matter of doubt, and though we may say that they have many resemblances to the enzymes, this does not carry us much further. It has been supposed by some that they are of a proteid nature, and they have been divided into toxalbumins, toxalbumoses, toxo-globulins, &c., according to their characters. But there is reason to believe that the true toxic substance clings very closely to any proteid material which may be in its neighbourhood. Hence, a toxalbumose, for example, may really be nothing more than an entanglement of the true toxin with an albumose formed as the result of the peptonising action of another product of the micro-organism upon the proteid in the midst of which the micro-organism which produced both has been living.

In a certain measure, the toxins may be likened to ordinary chemical irritants; but here again the point that the bacteria which form them grow and multiply gives to them a special importance. For though, like other chemical substances, the toxins are excreted by the kidneys or other eliminating organs, the laboratory in which they are produced is in the body, and fresh quantities are constantly being formed to replace those which disappear. Nor does the action of the toxin cease with the actual death of the cells with which it comes into contact, for these cells and the substances which result from their disintegration in their turn act as irritants. So the vicious circle is kept up until the amount of toxin is so large and the resisting powers of the body are so undermined that the animal dies, or until some factor intervenes to set a limit to the multiplication of the micro-organism and its production of toxin.

Animal causes of inflammation are relatively uncommon, and seem to act more after the fashion of a non-living irritant than might be supposed. They differ from the bacteria chiefly in the point that, so far as is known, they do not produce any substances comparable to the bacterial toxins. In cases where the animal irritant acts upon the skin, the inflammation is often nearly as much due to the dirt &c. which coincides with their presence as to the parasites themselves. In the case of parasites which are present within the tissues, on the other hand, the inflammation which supervenes is usually very trifling; the sequels of the inflammation produced may however be considerable. It is of course obvious that the inflammation following upon the sting of an insect depends upon a non-living chemical irritant, but it may be mentioned that a bacterial irritant may be introduced into the tissues along with the venom. Many of the animal venoms, like the bacterial toxins, give the albumose reactions.

TYPES OF INFLAMMATION

It will readily be understood that since the nature and the variety of the irritants which lead to inflammation show so many differences, there must be a corresponding number of variations in the type of inflammation set up. It cannot be expected that the effects of an application of a moderate degree of heat will produce the same picture as that resulting from the impact of a bullet, or that either of these will not differ from the picture yielded by the local action of a rapidly growing micro-organism. So, too, the effects of applying turpentine, for example, to the skin will not be expected to produce the same effect as the application of the same drug to the kidney, which is a far more vulnerable tissue than the skin.

But it is also clear that all differences in the type of inflammation must depend upon what may be termed the animal factors as distinguished from the irritant which acts upon those factors. We have seen that in inflammation a series of changes occurs which concern the blood-vessels, the leucocytes, the red blood corpuscles, and the essential elements of the part in which the inflammation is taking place, and we must conclude that any variations in the type of inflammation must depend upon changes in one or other of these factors.

To certain of these points passing reference has been made already. It has been said that the amount of the exudation may vary between wide limits according as the tissue in which the inflammation is taking place is loose or rigid. So, too, the degree to which the blood-vessels have been damaged, and the degree, in consequence, to which they allow of the escape of red blood corpuscles, vary in different cases. Nor is the number of leucocytes that migrate through the vessels always constant, nor the amount of degeneration which is undergone by the essential elements of the inflamed part, nor the pain experienced.

It is therefore customary to define the term more exactly whenever that is possible, and an inflammation is spoken of as hæmorrhagic, spreading, specific, acute, chronic, serous, suppurative, and so on. At the same time it has become the custom to indicate the occurrence of inflammation in a tissue by the affix 'itis,' so that we find the terms osteitis, nephritis. pericarditis, meningitis, synovitis, myositis, neuritis, dermatitis, &c. Yet a third set of terms has been introduced to indicate the particular cause of the inflammation, so that we have the names rheumatic, tuberculous, syphilitic, erysipelatous, &c.

Many of these terms are very useful, and in particular those which have reference to the anatomical characters of the condition ; those which profess to give the etiology are only valuable when the cause is actually known, when it is merely surmised they are often misleading.

Certain of the terms applied to inflammation are of sufficient importance to deserve special mention. These terms are 'infective,' 'specific,' 'acute,' 'chronic,' 'interstitial,' 'parenchymatous,' and 'catarrhal.'

(*a*) An **infective** inflammation is one which can be conveyed from individual to individual ; the disease known as diphtheria is an example of a typically infective inflammation. Infectivity depends upon the fact that the irritant which causes the inflammation is a living micro-organism ; it can multiply and form its toxin wherever it finds the food it requires for these purposes, and hence, if a portion of material containing some of the bacteria which caused the inflammation in the first individual be conveyed to the second, it is able, *cæteris paribus*, to induce a similar inflammation in him also, and so on *ad infinitum*. In the case of diphtheria we have identified the irritant as a bacillus having certain definite characteristics, and the same is true in the case of several other infective diseases. But in several instances, though we have plentiful clinical evidence that the disease spreads from one individual to another, the actual cause of the disease has not been discovered. An example of this kind is afforded by syphilis, and we include syphilis among the infective inflammations, prematurely, it is true, from a strictly scientific standpoint, but with none the less certainty that our assumption as to the nature of the disease will sooner or later be justified by the discovery of the organism which causes it.

(*b*) A **specific** inflammation is one which has special characters by which it can be differentiated from other forms of inflammation. The chief of these differentiating points is that the cause of the inflammation is always one and the same variety of micro-organism. Thus tuberculosis is a specific inflammation which is caused by a specific micro-organism, the bacillus tuberculosis. And though the bacillus itself and the inflammatory lesion which it produces have many points in common with other bacilli and the lesions they produce, yet they have certain special characters by which they can be recognised with sureness. It is not in all cases, however, that the question is so simple as it is in tuberculosis. Sometimes a disease and its manifestations are spoken of as specific from the anatomical side alone. Syphilis is here again an example. There are certain points about the appearances of the lesions of syphilis, both macroscopic and microscopic, and about its distribution in the body, which justify us in separating the syphilitic inflammation from all others, in spite of the fact that the crucial point of difference is still undiscovered. The existence of specific forms of inflammation depends upon the fact that the organisms which cause them form specific toxins.

(*c*) The term **acute**, as applied to inflammation, has rather a clinical than a truly pathological significance. It implies that some or all of the cardinal signs are well marked, and that they have manifested themselves with great rapidity. Thus the inflammation which follows the sting of a bee is typically acute. In strict pathological parlance an inflammation may be severe or slight, may be widespread or confined to a minute area, but it cannot be differentiated from other forms of inflammation by its acuteness, because all inflammation is acute. When an irritant acts on a given point, the effects which it produces vary in intensity according to the strength of the irritant, there is less or more tissue destruction, a smaller or greater area comes beneath the action of the irritant, but the changes which it induces in the blood-vessels, the leucocytes, and the tissue cells commence directly these elements feel the effect of the irritant. From a clinical point of view, however, the term is a valuable one.

(*d*) The term **chronic**, as applied to inflammation, is one which needs careful consideration. It is clear that a chronic inflammation is one which persists for a long time, but it has just been said that every inflammation is acute, and the two statements are difficult to reconcile.

Now, every inflammation consists in the establishment, in response to an irritant, of a series of vascular changes, a more or less extensive migration of leucocytes, and a more or less extensive destruction and degeneration of tissue cells. So soon as these conditions are established the inflammation is in existence, but no sooner is the condition brought about than it turns towards one of two directions. Either the irritant ceases to act, or it continues to act. In the former instance the whole process of inflammation retrogresses; the blood-vessels return to normal, the migrated leucocytes are carried along the lymph-stream to the nearest lymphatic glands, such tissue elements as are irreparably damaged are removed, and such as are not irreparably damaged recover. This whole process is known as *resolution*, and it may be regarded as a *physiological* termination of inflammation. If the irritant continues to act, the phenomena of inflammation continue to be manifested until the results which they occasion are so marked that they lead to the appearances known as *suppuration*, *ulceration*, &c., and these may be called the *pathological* sequels of inflammation.

Further, it is clear that whenever inflammation has been produced, there is always a necessity for the occurrence of regeneration and repair in the part in which the inflammation has taken place. For reasons that it is unnecessary to discuss here, regeneration and repair can only take place at a spot at which inflammation has ceased, but it is not impossible that an irritant may be producing inflammation at a spot some little distance from another spot at which the absence of irritant action allows the regenerative and reparative processes to proceed.

Hence it is not impossible that in the same microscopic section we may find one focus of acute inflammation, and a short distance off another focus, at which there are evidences of repair; foci of migrated leucocytes at one place, foci of young reparative tissue at another close by. Now if the inflammatory portion of the entire picture gains the upper hand, the whole passes into one of the pathological sequels of inflammation, and if the reparative portion gains the upper hand, the whole becomes converted into a physiological sequel of inflammation. But if the two portions—inflammatory and reparative—are so closely balanced that neither gains the upper hand, we get a macroscopic picture of an inflammation, which lasts for a considerable time, and may, therefore, with justice be called chronic, and a microscopic picture of inflammation and repair in close proximity with one another.

Such a condition as that which has been sketched out above is not, however, the only one to which the term 'chronic inflammation' has been given, though it is only in this sense that it will be used in the present work. By many authors it has been used to denote a condition in which there is a great increase of the fibrous tissue of an organ, a condition which we shall call **chronic fibrosis.** It will appear later that the chief method by means of which repair is carried out is the new formation of connective tissue, and it has been assumed that wherever an increase in the amount of connective tissue in an organ is recognisable, it is evidence that its formation has been preceded by inflammation. And since this newly formed connective tissue is only formed with great slowness and in the comparative absence of any signs that it is being formed, the process has been considered as an eminently chronic one. The additional epithet **interstitial** is often given, so that the expression **chronic interstitial inflammation** is one to which these authors attach a very definite meaning.

(*e*) The terms **interstitial** and **parenchymatous** may be taken together for consideration. In any of the more complex tissues, e.g. a gland, one can distinguish between the true functionating elements of the tissue and the supporting structures. To the former the term 'parenchyma' has long been given, and to the latter the term 'interstitial tissue.' The names are objectionable from many points of view, but they are so firmly established that it is, at present, impossible to dislodge them.

When the expressions 'parenchymatous' and 'interstitial' inflammation were used, they were meant to express that in the one instance the essential elements of the organ were the seat of inflammation, and in the other that the inflammation was confined to the supporting structure alone. It is now known that such a differentiation is impossible. For since inflammation is a process which is intimately bound up with the blood-vessels, and since all blood-vessels run in interstitial connective tissue, every inflammation must, by its very nature, be an interstitial process. And since every irritant must produce degenerative changes in the cells upon which it comes to act, every inflammation must also be parenchymatous. It is true that in an organ like the kidney, where the essential elements largely outweigh the supporting structure in amount, the effects of irritant action will be characterised by a very extensive change in the renal epithelium, and that the connective-tissue changes may escape notice altogether, while in the case of a tendon the exact opposite will obtain. But this does not mean that the interstitial tissue in the one case, and the connective-tissue cells in the other, escape, for by the very nature of the process this is impossible.

The term 'parenchymatous inflammation' is less objectionable than its fellow owing to the special meaning which has been attached to the term 'interstitial inflammation.' It will be necessary to revert to this question when we come to consider chronic fibrosis.

(*f*) **Catarrhal inflammation** derives its name from the fact that its most typical example is found in the condition which is known as catarrh from the fluidity of the secretion by which it is accompanied.

If we consider the phenomena which constitute a 'cold in the head,' we shall remember that the first condition is one of extreme dryness of the mucous membrane of the nose and throat, conjoined with a certain amount of actual pain. After a short time this dryness gives place to the formation of an excessive amount of secretion, which is at first watery but which soon becomes thick, yellow, and tenacious. In course of time this secretion, which is at first copious, diminishes, and recovery is complete.

The differences in the character of the secretion correspond to differences in its composition. At first the secretion consists of little else than watery exudation from the inflamed blood-vessels of the mucous membrane. At this time cells are few in it, so that the secretion is limpid, but the albuminous nature is well shown by the stiffening which it affords to the handkerchief when dry. As the condition progresses, the number of cells in the secretion increases, but the greater number of these are not leucocytes which have migrated through the vessel-walls, for the inflammation is one of little intensity. The bulk of the cells are desquamated epithelial cells derived from the surface of the mucous membrane. As the result of the excessive amount of blood which the mucous membrane receives, the irritation and stimulation, the epithelial cells proliferate rapidly and are rapidly thrown off. At the same time the cells exercise their normal function, viz. the formation of mucus, to an abnormal and excessive degree. Hence the fluid that exudes from the blood-vessels becomes mixed with a large number of epithelial cells and a large amount of mucus. In addition it contains a fair proportion of migrated leucocytes.

Characters such as have been described in the preceding paragraph are common to all forms of inflammation in which a mucous surface is involved, so that the variety of inflammation which originated in a special example has now been recognised as a characteristic of mucous membranes, and the name which was first given to a special example has been utilised for the whole group. Whether we meet with an inflammation of the bronchial tubes, or of the urinary bladder, or of the intestines, we have to do with an inflammation of a mucous membrane, and *cæteris paribus* the characters of the inflammation are in all cases the same.

The expression 'catarrhal' has been used very largely in contrast to an inflammation which has been termed **croupous**. The latter term has now largely fallen into disuse, but it is still not uncommon to hear the form of pulmonary inflammation which affects entire lobes of the lung spoken of as 'croupous pneumonia.' The origin of this term lay in the recognition of a form of inflammation of the fauces which was called **croup** or **membranous croup**, and since the histological characters of the faucial and the pulmonary forms of inflammation were closely similar, the term 'croupous' was given to the entire variety. It is characterised by the fact that the exudation has a great tendency to coagulate, with the result that strands of fibrin are to be seen traversing the inflammatory mass.

We now know that these appearances denote nothing more than an excessively severe form of inflammation, and since the term 'croup' has largely lost its significance owing to recognition of the fact that most, if not all, cases of what a previous generation of pathologists would have called croup, are examples of diphtheria, the term 'croupous' as applied to inflammation has fallen into disuse. For it is certain that this variety of inflammation, which we may term **fibrinous** if we wish, has no necessary connection with the disease known as diphtheria.

SECTION III

THE SEQUELS OF INFLAMMATION

From the description of inflammation that has been given in the preceding section, it appears that we must look on the process as a condition of unstable equilibrium; it is no sooner established than it tends to take some other direction. We must now proceed to consider the sequels of inflammation. These sequels may be divided into two great classes—physiological and pathological.

A.—RESOLUTION

When an irritant ceases to act, the inflammation to which it gives rise at once commences to recede. The amount of fluid poured out by the blood-vessels is now no longer in excess of the amount of lymph which flows away by the lymphatics, but the exact contrary obtains. As a consequence, the swelling at once begins to diminish, and since this diminution in swelling reduces the pressure upon the nerve fibrils, the pain becomes less severe. The congestion and increased temperature disappear more slowly, and the latest to recover is the function. For a long time after resolution has taken place, the former seat of inflammation is, however, in an altered condition so far as its nutrition is concerned. This can be seen by the readiness with which slight injuries set up a fresh attack of inflammation in a part which has only recently recovered from a previous attack. Ultimately, an inflamed part in which resolution has taken place—if the resolution has been complete—returns to a perfectly normal condition. Resolution, therefore, is the simplest physiological sequel of inflammation.

Simple resolution of an inflammation is a common phenomenon among the minor ailments of life. As an example the course of an ordinary cold (coryza) or a conjunctivitis contracted by exposure to a draught may be cited. In either case as soon as the inflammation has reached its height, it commences to recede, and the mucous membrane implicated returns in a short time to its original condition. Simple resolution also occurs in the case of some of the more severe diseases. Thus it forms the termination of a large proportion of cases of lobar pneumonia and erysipelas, measles, and scarlatina. The tendency, however, is for the severer forms of inflammation to be accompanied by one or other of the pathological sequels, and then resolution, if it occurs, is a much less evident process, since it is overshadowed by the much more obvious process of repair. Thus, if the inflammatory processes which constitute typhoid fever, tuberculosis, syphilis, glanders, small-pox, and many others, terminate in recovery, the tissue in which the inflammation has taken place is never left in exactly the condition in which it was before the inflammation occurred.

This brings us to the point that resolution, and repair, and regeneration may take place, not as direct terminations of inflammation, but after the occurrence of one or other of the pathological sequels. It is true that resolution, and repair, and regeneration commence directly the inflammatory action ceases—that is, so soon as the irritant ceases to act—but the irritant often persists in its action, and even if the original irritant ceases to act, it has commonly given rise to the appearance of a multitude of subordinate irritants in the form of dead and disorganised tissue cells, pressure of exudation fluid, &c. There is, therefore, a great tendency for irritant action to persist and keep up the inflammation, with the result that conditions are produced which may be spoken of as the pathological sequels of inflammation. To these we shall now turn our attention, and after they have been described, we shall return to the physiological sequels of regeneration and repair.

B.—SUPPURATION. ABSCESS AND ULCERATION

Suppuration is an inflammatory process which consists in the production of pus (p. 53). It is, fundamentally, an excessive manifestation of the same phenomena which are integral portions of inflammation. Consequently, it is not difficult to conclude that suppuration depends upon persistence of irritant action, and since the irritants which manifest persistence of action in the highest degree are bacterial, there is an *a priori* presumption that the causes of suppuration will be found to be of this nature.

The whole question of suppuration received a great deal of attention about twenty years ago when it first began to be recognised that bacteria play an overwhelmingly important part in the causation of disease. It is unnecessary to refer to the large amount of work that has been done on the subject of the micro-organisms and suppuration, to the discussions as to whether pus could be formed in the absence of bacteria or to the other kindred work that is, at the present day, summed up in the antiseptic and aseptic treatment of wounds introduced by Lord Lister. It may be stated in few words that the modern view of suppuration is that it may certainly be the result of the action of an aseptic non-bacterial agent (e.g. turpentine, nitrate of silver), but that in the overwhelming preponderance of cases it is the result of bacterial action. It is also agreed that it may result from the presence of the dead bodies of bacteria, apart from their toxin, but it is universally held that this explanation of its formation is one which is but rarely applicable outside the laboratory, and that for all practical purposes the existence of suppuration must be regarded as an expression of the irritant action of living, multiplying, and toxin-producing micro-organisms.

Just as all kinds of micro-organism may, theoretically, lead to inflammation, so theoretically all kinds of micro-organism may lead to suppuration. Practically, however, there is a limitation in both cases; some bacteria produce a toxin so weak, or the conditions of their multiplication are such, that when they gain access to the tissues they are destroyed before they are able to do any harm; others are so virulent that they form a sufficient amount of toxin to kill the animal before there has been time for inflammation or suppuration to manifest itself. This limitation is particularly the case with suppuration, and it is a relatively small number of varieties of bacteria that are found to be at all frequently present in pus, i.e. that cause suppuration.

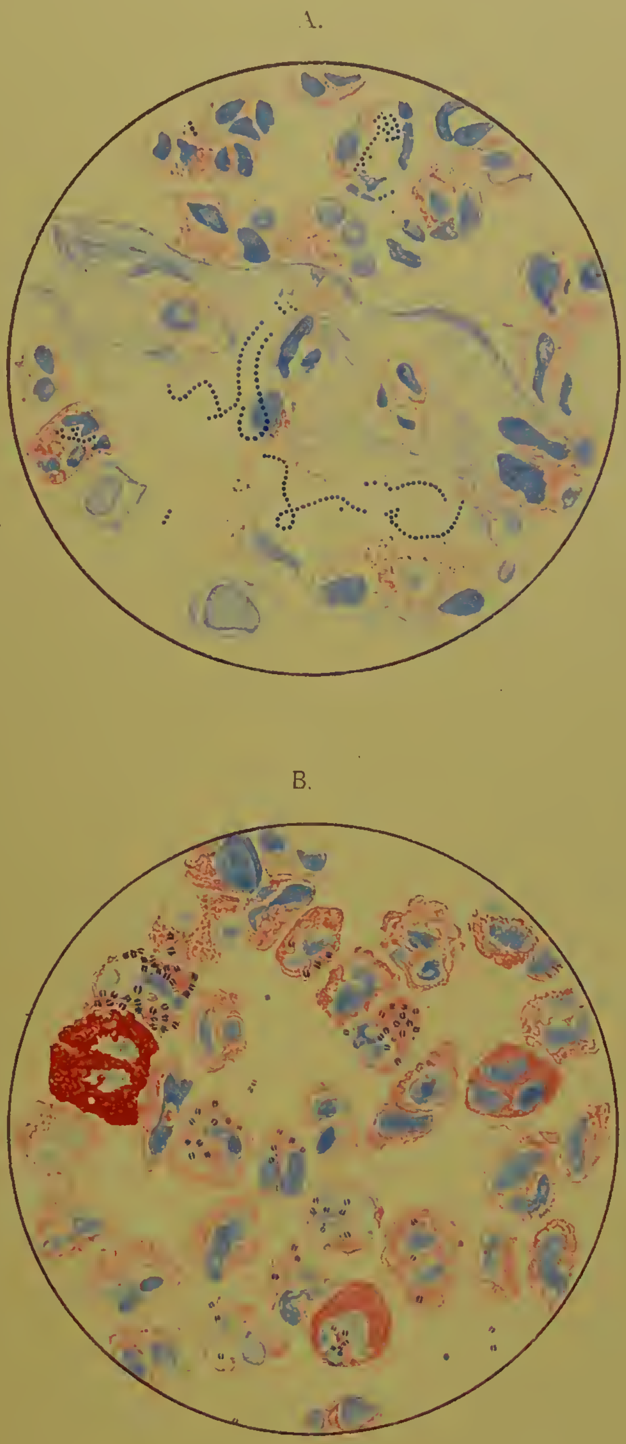
Most of the bacteria of suppuration are micrococci, and the association of suppuration with the presence of these particular micrococci is so common, that they have been collectively termed the 'pyogenetic cocci.' The group of pyogenetic cocci consists of the following members: *staphylococcus pyogenes aureus*, *staphylococcus pyogenes albus*, *streptococcus pyogenes*, *micrococcus pneumoniæ*, *micrococcus gonorrhœæ*. Besides these cocci certain bacilli are not unfrequently the cause of suppuration. By far the most important is *bacillus tuberculosis*, but *bacillus typhosus*, *bacillus mallei* (*glanders*), *bacillus pyocyaneus*, and a few others are also causes of pus formation. Actinomyces, one of the true moulds, is a somewhat rare, but a very important member of the pus-forming organisms, and several others of the group of

PLATE IV

Fig. A.—Coverslip film of pus from an acute abscess. Across the film is a strand of albumin which has been coagulated in the process of hardening. The disintegrating nuclei of several pus cells are visible, and some of them show a small quantity of granular material (stained pink), which represents the granules of the finely granular oxyphil cells of the blood. Below and to the left of the figure are two hyaline cells. Short and long chains of streptococci (str. pyogenes) are present, and upon these the formation of the abscess depended. Film hardened by heat, stained by watery eosin and watery methylene blue, and mounted in Canada balsam. Magnified about 800 diameters.

Fig. B.—Coverslip film of pus from a case of gonorrhœa. Numerous pus cells richly provided with fine oxyphil granules are present, together with one coarsely granular oxyphil cell showing large and brilliant granules. Many diplococci (gonococci) are visible, of which the great majority are situated within the pus cells. In the case of those that are extra-cellular the existence of a capsule is to be noted. Method of preparation and magnification the same as in fig. A.

Plate IV.



Micro-Organisms in Pus.

streptothrices—filamentous moulds concerning which we know very little—appear to possess the same property.

When any of the pyogenetic micro-organisms have led to the formation of an appreciable amount of pus which is confined in the depth of the tissues, the resulting focus of suppuration is termed an *abscess* in general terms. But in many instances special names are given. Thus a collection of pus in the pleural cavity is called an *empyema*, in the pelvis of the kidney a *pyonephrosis*, in the fallopian tube a *pyosalpinx*, in the anterior chamber of the eye a *hypopyon*, and *whitlows*, *boils*, *furuncles*, *carbuncles*, are simply forms of suppurative inflammation having rather special characteristics.

The actual method by which an abscess is formed is somewhat as follows. When the micro-organisms have reached a certain point, it may be by direct introduction into the tissues or it may be by being carried thither along the blood stream, they commence to multiply. At the same time they form their specific toxin, and this acts upon the tissue elements with which it is in contact, leading to their degeneration and death. By this means a certain amount of proteid material is provided for the nutrition of the bacteria while they continue to multiply and form toxin. The two processes, therefore, toxin formation and destruction of tissue cells, tend to extend in ever-widening circles, and were it not that the tissues themselves oppose an obstacle to their own degeneration and destruction, the process would go on until life of the animal was impossible. But the very irritant action of the bacteria themselves and their toxin leads to those vascular and cellular changes which we call inflammation, and there consequently arise a series of forces in the parts around the spot at which the bacterial activity is going on, which is destined to combat the bacterial activity. Fluid collects around the minute colony of bacteria and there coagulates, while leucocytes, obeying the laws of chemiotaxis, flock thither in large and ever-increasing numbers. Acted upon by the bacterial toxin, multitudes of these leucocytes die, but multitudes are able to resist and, by the aid of phagocytosis, englobe numbers of the bacteria. Whether the phagocytes are able to englobe and digest fully living and virulent bacteria is a matter of uncertainty, but there is no doubt that a large number of the bacteria succumb and are found inside the leucocytes (Plate IV, B).

So far we have accounted for the presence of the cells and the bacteria in pus, but it has not appeared how the liquefaction of the coagulated exudation fluid is brought about. The facts that pus contains albumoses and that it is commonly not auto-coagulable, indicate that the proteid substances from which it is formed have undergone peptonisation. It has already been said that certain of the bacteria form peptonising enzymes as the result of their life-history. *Staphylococcus pyogenes aureus* is of this kind, and since it is undoubtedly the commonest bacterial cause of suppuration, there is no difficulty in understanding how the necessary liquefaction in the formation of the abscess is brought about. But the matter is not quite so simple. For *streptococcus pyogenes*, an organism that does not fall very far behind *staphylococcus aureus* in the frequency with which it is found as a cause of suppuration, does not form a trace of peptonising enzyme. We are therefore compelled to look in some other direction, and it is probable that the answer to the question is given by the leucocytes. We know that they—or certain of them—act as phagocytes, that in the pursuance of this function they digest such digestible substances as they take into their bodies. We have ample evidence that the removal of such substances as bone, to say nothing of softer substances, is carried out by their means. We know that the only way by which such removal can be carried out is that of solution, and it is not difficult to conceive that in the liquefaction of the dead and coagulated material which collects around a focus of pyogenetic micro-organisms, the leucocyte plays a fundamental part.

An abscess, then, formed after the manner which has just been described, consists of a number of zones which gradually merge into one another. In the centre there is a larger or smaller amount of liquid pus; around this there is a zone of material which is just on the point of breaking down into pus, but which is as yet solid; it used formerly to be called the 'pyogenic membrane;' more distally there is a zone in which the phenomena of inflammation are in full swing, and this zone passes, through concentric zones of regeneration and repair, into the fully normal tissues around.

The pus in an abscess is confined within its walls under a certain amount of pressure, and from its nature is of course subject to ordinary hydrostatic laws. That is to say, pus tends to travel in the direction of least resistance, whatever that may be. This feature in connection with abscess formation is known as 'pointing,' and it is the general, though not the universal, rule that an abscess points in some particular direction. Thus an abscess in the subcutaneous tissue points towards the skin; an abscess formed in connection with the lower dorsal or upper lumbar vertebræ may pass along with the nerves forming the lumbar plexus, into the psoas muscle, and following the course of that muscle, point in the thigh, or it may burrow among the lumbar muscles and point in the back; an abscess in the lung may burst into a bronchus or it may point towards the pleural cavity, and on the contrary, an empyema may burst into the lung or into the stomach after travelling behind the crura of the diaphragm, and so on. The actual pathology of pointing is simply a special example of the pathology of pressure atrophy, the tissues being absorbed in front of the advancing pus in exactly the same manner as they are absorbed in front of an advancing solid growth.

The formation of pus does not, however, always lead to the formation of an abscess. If the focus of suppuration is situated upon a surface, such pus as is formed is carried away before it is possible for an accumulation to take place. This is typically the case in suppurative conditions of the intestine such as dysentery, and, indeed, in all cases in which ulceration is present. For an ulcer is nothing else than an open abscess, and there is no better way of gaining a conception of the characters of an ulcer than by considering the appearances that would be presented if an abscess were bisected. There is in it the same disintegration of tissue which breaks down into a liquid material and flows away (the pus), the same layer of tissue infiltrated with leucocytes and coagulated exudation fluid which is ready to break down into pus, and the same congested inflamed zone, and regenerative and reparative zone beneath them all. In fact, when an abscess has pointed and burst, it is nothing more than an ulcer; an ulcer, it is true, which has a base somewhat further removed from the surface than the ordinary ulcer, and an obviously exposed surface somewhat less extensive, but a true ulcer none the less.

When an abscess or an ulcer is formed in close connection with a mucous membrane, the inflammation which accompanies the suppurative process leads to a morbid activity of the mucin-forming cells with the result that an excessive amount of mucus is produced. This mucus becomes mixed with the pus, and is, in many instances, the cause of that 'ropiness' which is so constant a characteristic of pus when a small amount of a caustic alkali has been added to it. In other instances there is no reason to implicate a mucous membrane, and then it is probable that the ropiness depends upon the presence of nucleo-proteid; an example of the latter kind is afforded by the pus found in a psoas abscess.

In the formation of the pus which flows from off the surface of an ulcer or is formed in the cavity of an abscess, the actual tissues of the part in which the suppuration is taking place are broken down into microscopic particles. This form of local death is known as **molecular necrosis**, and it is the typical way in which destruction of tissue takes place in suppuration. It is clear that either soft or bony material may become disintegrated in this way, and it would perhaps be well if the same term had been applied to molecular disintegration of both kinds of tissue. As a matter of fact, however, the term has been reserved for the soft tissues, and the similar change when it occurs in bone is termed **caries**.

When the irritant is very intense, or when there is some special factor at work which causes the blood supply of the part attacked by the irritant to be very small, the disintegration of tissue may not be molecular, but whole masses of tissue may die. Here we have a condition akin to gangrene, but the change is not known by that name, and here, again, we have different names according as the tissue which dies is soft or bony. If the mass of dead tissues is soft it is called a **slough**, but if bony a **sequestrum**.

A slough or a sequestrum may be of any size, from a mass so small that it is little more than perceptible by the naked eye, to a mass as large as the entire pancreas or the whole shaft of the tibia. Naturally the effects which necrosed portions of tissue have upon the entire suppurative process differ according to the size of the dead piece of tissue in question. It any case it must act as an irritant, and moreover, in a very large number of cases it acts as an irritant of considerable virulence, because it is a focus in which multiplication of bacteria is going on with great activity. But in addition its mere mass is a very important factor. For however we may regard the processes of inflammation and suppuration, it is certain that regeneration and repair cannot take place so long as the dead mass acts as an irritant, and therefore that the length of time that will elapse before repair is complete must be dependent in very large measure upon the size of the mass with which the repairing tissues are called upon to deal. For the same reason it is clear that the denser the mass of necrosed tissue, the longer this time will be, so that it is longer in the case of tendon than in that of loose connective tissue, longer in the case of bone than in the case of tendon. In the case of bone, indeed, where the sequestrum is of very large size, it is often quite impossible for Nature to effect its removal unaided by the surgeon's art, the more so since, as we shall see presently, she actually hampers her own work by partially enclosing the dead bone with bone of new formation (cf. fig. 15).

In all but the rarest instances the formation of a sequestrum is the result of some infective process taking place, either in connection with the bone-marrow or the periosteum, so that the conditions are eminently favourable for the formation of pus. Being situated in the deeper tissues this pus constitutes an abscess, points, and ultimately bursts. But since the factor which originally led to the institution of the suppurative process is still at work in the neighbourhood of the bone, and is, moreover, reinforced by the sequestrum itself, the formation of pus continues, and the pus itself finds its way to the exterior along the track produced by the pointing of the original abscess. This track in course of time becomes well worn, and, however devious its course, always opens on some free surface—usually the skin, and always leads down to some dead material—usually bone. It is then termed a **sinus**.

Owing to the fact that a sinus may fairly be regarded as a somewhat specialised portion of an abscess, and because its walls are constantly being irritated by the pus and other morbid products that pass over them, the histological elements present in the walls of a sinus are very similar to those present in the walls of an abscess. If a section be made of a sinus transversely to the axis of the lumen, that part of the wall which lies next to the lumen is seen to consist almost entirely of small round cells of the leucocyte type with very little supporting material. These cells readily fall into the lumen of the sinus, and contribute to the formation of pus; this layer is in every respect analogous to the inmost layer of an abscess. Further out there is a zone representing ordinary inflammation, but this is usually not very extensive. Still further out is a zone of tissue which we shall have to consider more fully later—granulation tissue—and around this again lie the normal tissues. The amount of granulation tissue in the wall of a sinus varies considerably, the chief factor in causing the variation being the length of time that the sinus has been in existence; when the sinus has been a long time in existence the amount of granulation tissue is great, and *vice versa*. The lumen of a sinus is commonly little more than a potential one, so that in a microscopic section it usually appears as a crevice or chink. This is due to the contraction of the surrounding tissues.

The orifice of a sinus upon the skin is sometimes very difficult to find owing to its small size, but still more owing to the fact that its edges are surrounded by soft and protuberant lips. These lips consist of granulation tissue, and their exuberance is due to the lack of resistance with which they meet, combined with the fact that they are constantly kept moist by the fluid which exudes through them. Sometimes the orifice becomes actually closed by the growth over the orifice of epithelium that encircles it. This epithelium is invariably unhealthy, however, and readily breaks down on the slightest pressure, whether of a probe or of the pus which collects beneath it.

Malignant ulcers.—We have said that an ulcer is essentially nothing more than an abscess which is open on the surface, and this is true of all inflammatory ulcers. But it is common to use the term in connection with certain of the degenerative changes that occur in the malignant new-growths, and here the pathological appearances have many points of difference from the form of ulceration we have just been considering. In the first place, malignant ulceration is an entirely non-inflammatory process. It consists solely in a degeneration and disintegration of a part of the growth, and the blood-vessels of the tumour, if they take any part in the process, undergo changes quite unlike those which are characteristic of inflammation. And in the second place there is, beneath the malignant ulcer, no regenerative and reparative zone such as that which we have seen forms a constant adjunct to the true ulcerative process. As a matter of fact the malignant ulcer is formed as the combined result of a pressure atrophy of the tissues in which the tumour is growing, and which lie superficially to it, and a degeneration, generally fatty, of the most superficial portions of the tumour itself, dependent upon the irritation to which they become exposed by the removal of their coverings. It thus follows that malignant ulceration is most commonly found in situations where the chances of irritation are especially great, e.g. the epidermis, the entire alimentary tract, the uterus, cervix, and vagina. It is needless to insist upon the very important part that is played by bacteria in aiding and perpetuating malignant ulceration. In this respect there is little difference between malignant and inflammatory ulceration. Nevertheless the influence of bacteria upon malignant ulceration is greater than their influence upon inflammatory ulceration, because the various defensive mechanisms which tend to hold inflammatory ulceration in check, and to nullify the irritant, do not come into play to the same extent, and many of them not at all, in the case of malignant ulceration. (Cf. fig. 154.)

The absence of a regenerative and reparative zone beneath the malignant ulcer is the explanation of the fact that a malignant ulcer when once formed never repairs like the inflammatory ulcer, It can only remain stationary or become larger, and it almost invariably takes the latter course.

There is one apparent exception to this statement, but it is apparent only. Sometimes a new-growth, or a portion of one, ulcerates freely, and the original situation of the tumour becomes filled up with scar-tissue. Cases of this kind are very rare, but they are the foundation of the treatment of cancer and other new-growths with acids and other corrosives. What really happens in these cases is that the destruction of the tumour has been carried out until the normal, or relatively normal, tissues underlying the tumour have been laid bare. Under these circumstances it is obviously not fair to speak of a *malignant* ulcer, and the repair which takes place is as definitely a sequel of inflammation as the repair which takes place after a typhoid ulcer has been formed.

The changes which we have hitherto described as pathological sequels of inflammation have been all characterised by the fact that they are accompanied by the formation of pus. In another set of pathological sequels the formation of pus, though a frequent accompaniment, is not essential. Of this class gangrene is the typical example, but we shall not do more than refer to it here, since the whole subject of local death has already been discussed (p. 28 *et seq.*). Among the varieties of local death we may also place that molecular necrosis which we find in ulceration, if we so wish, together with those forms of local death represented by the names 'slough,' 'sequestrum,' 'caries,' &c. Upon consideration it will be clear that the dry form of gangrene is never met with as a sequel of inflammation. The reason of this is that the ultimate cause of the gangrene is always pressure on the veins by the accumulation around them of the exudation products of inflammation, or else direct thrombosis of the veins themselves as the result of penetration of their walls by the inflammatory process.

We may now return to the consideration of the physiological sequels of inflammation.

Leaving out of consideration that part of the process of resolution which consists in the removal of the excess of exuded fluid and of migrated leucocytes, as having no immediate relation with the subjects we are about to discuss, it is clear that resolution can only be concerned with such of the essential cells of an inflamed part as have not been damaged past recovery. If recovery is possible when the action of the irritant ceases, the cells will recover; but if this is not the case, they will degenerate and die, and then the subsequent history of the part depends upon whether regeneration takes place or repair.

C.—REGENERATION

The method whereby regeneration of cells takes place is by cell division. It will be remembered that two methods of cell division are known, the direct (amitosis), and the indirect (mitosis). In amitotic division the nucleus simply divides into two equal segments each of which becomes the nucleus of a new cell, the protoplasm of which is formed by a constriction of the hypertrophied protoplasm of the mother cell. In mitotic division the nucleus divides by the process of karyokinesis, and when the two daughter nuclei are formed a constriction takes place in the protoplasm of the mother cell as in the other mode of division. Both of these methods are known to occur under pathological conditions, and if we may conclude from the relative frequency with which karyokinetic figures are to be seen in the cells of rapidly growing tumours, &c., the mitotic mode of division is commoner in pathology than in physiology.

Regeneration does not take place with equal frequency in the case of all kinds of cell. In some—e.g. squamous epithelial cells—it is the rule, one might almost say the constant rule; in others—e.g. ganglionic cells of the nervous system—it is probable that once a nerve-cell has been destroyed it is never regenerated. Between these two extremes lie the bulk of the cells of the body. It will, however, be advisable to take the various kinds of cell individually and consider in the case of each how far regeneration occurs.

(1) **The epithelia.**—Among the epithelia regeneration is of common occurrence. In the case of squamous epithelium it is practically constant. When a portion of this kind of epithelium has been destroyed the still living cells of squamous epithelium round the focus of destruction commence to divide in their deepest layers (germinal layer). They divide by partitions at right angles to the raw surface and gradually encroach upon it all round. But besides dividing at right angles to the plane of the raw surface, they also divide in a series of planes parallel with it, so that ultimately the spot at which the epithelium was

originally removed becomes again covered with a skin of normal thickness. Before this is complete, however, the edge of the investing epithelium is a shelving one and consists of a single layer of cells nearest to the centre of the raw spot and of increasing numbers of layers as one proceeds outwards to the normal skin. As a result of this arrangement the appearance of the growing edge of an investing epithelium is highly characteristic. It shows as a thin line surrounding the raw tissue which it is covering, red where it consists of a single layer, bluish where it is a few layers deep, and thence it merges into the normal colour of the skin around. With the naked eye the bluish portion of the line is easily perceptible, but the red part is more difficult to distinguish, though it is quite easy to see under the microscope. So far as we know there is no other method by which the epithelial covering of a part can be renewed than that which has just been described. In particular, the corium takes no part in the process.

It follows from what has been said as to the method in which the cuticular epithelial layers are renewed when they have been destroyed over any part, that if the surface over which the skin has been removed be considerable, its re-investment will take a long time. Any localised patch of epithelium may however become a centre for the regenerative process, so long as it consists of still living cells. Advantage of this fact has been taken in the clinical treatment of large surfaces denuded of epithelium by the process known as 'skin-grafting,' in which small portions of skin removed from healthy parts by means of the scissors are applied to the large denuded surface at different points. If the 'grafts' survive they become centres for regeneration of epithelium, and the time necessary for the covering of the whole raw surface is enormously diminished. Several conditions have to be fulfilled if the grafts are to live and increase in size, but one of the most important is that in taking the graft a portion of the germinal layer of the epithelium must be included in it.

Columnar epithelium also regenerates whether it be of the ciliated or the non-ciliated variety. But here a point must be noted which is of importance. Columnar epithelium is found in ducts and duct-like glands. And though there is abundant proof that the actual lining epithelium of these ducts and glands is capable of regeneration, it must not be inferred therefrom that the ducts or the duct-like glands, *considered as composite entities,* also regenerate. How far this latter condition obtains we shall consider shortly.

That columnar epithelial cells regenerate, the course followed by the columnar epithelium of the naso-pharyngeal tract during and after an ordinary coryza is sufficient evidence. For during the early stages of a cold in the head the columnar cells lose their cilia, undergo mucoid degeneration, and desquamate in large numbers, but when the return to health is complete the naso-pharyngeal mucous membrane is again found to be covered by a ciliated columnar epithelium containing goblet cells, of a completely normal character. Considering, too, the way in which recovery takes place from inflammatory conditions of the intestines and other parts which are lined by a columnar epithelium, there is little doubt that regeneration of epithelium takes place in these parts when necessary.

In the case of spheroidal epithelium, which is the type of a true secreting epithelium, it is perfectly normal for destruction and regeneration of epithelium to take place. Indeed, the actual secretion itself consists of the products of cell disintegration. This is typically the case in the formation of milk, and even where the cell forms granules which are cast out from the cell and form its secretion, as in the case of the pancreas, it is probable that a certain amount of actual disintegration and regeneration of the cells occurs. In the case of this variety of epithelium, also, a sharp distinction must be drawn between the regeneration of the epithelial cells themselves and the regeneration of the gland as a composite whole ; here we are only speaking of the epithelium.

(2) **The connective tissues.**—Regeneration of the connective tissues, after destruction, is a very widely spread phenomenon. It is, in fact, in the matter of one member of the group, viz. fibrous tissue, one of the very commonest sequels of inflammation ; for, as we shall see later, repair consists almost entirely in the formation of new fibrous tissue.

As might be judged from the differences that obtain between the different members of the connective-tissue group, and especially from their different rates of growth, regeneration is not met with equally commonly in all members of the group. When fibrous tissue has been destroyed a true regeneration of fibrous tissue takes place, and the same is true, as a rule, in the case of bone. Regeneration of cartilage, on the other hand, is of excessively rare occurrence if it occurs at all, so that when cartilage has been destroyed, repair and not regeneration takes place.

In spite of the differences between the members of the group, however, there is a considerable amount of interchangeability among them. But the interchangeability always, or almost always, takes place in the direction of the replacement of a higher member of the group by a lower. Thus, it is common for cartilage which has been destroyed to be replaced by fibrous tissue, and the same is true of bone, though less commonly. It is, on the other hand, very rare for injured or destroyed cartilage to be replaced by bone, though examples of this condition are known to exist. Bone, too, though it may be replaced by fibrous tissue, is probably never replaced by cartilage. It is doubtful what is the course taken when yellow elastic tissue has been destroyed; probably it is replaced, like the other members of the group, by ordinary fibrous tissue. Nevertheless, it has recently been shown that in the condition known as cirrhosis of the liver, there is a definite hypertrophy of the yellow elastic tissue of the organ (Flexner), and so it is not impossible that a true regeneration of this variety of the connective tissues may occur.

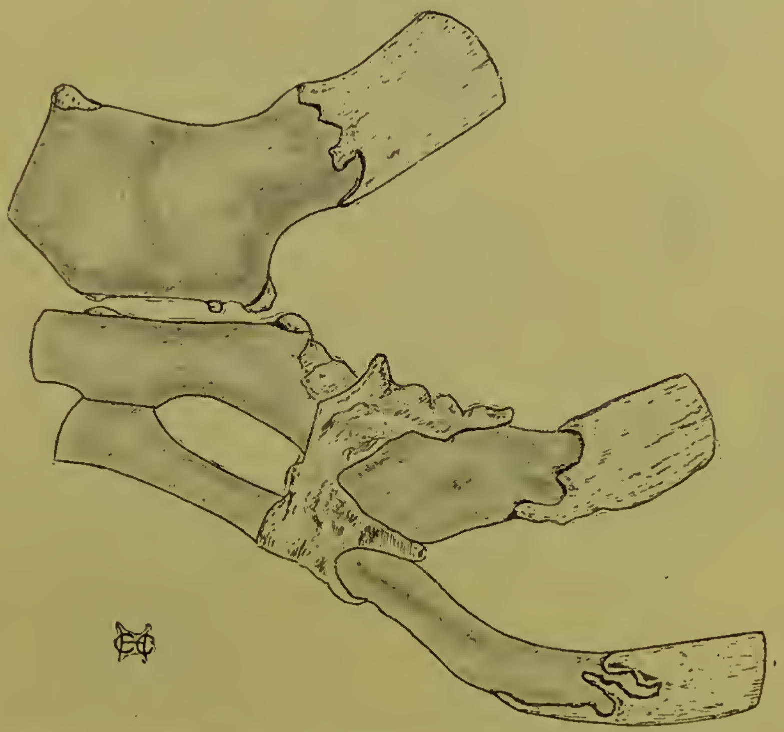


FIG. 14.—FRACTURE OF COSTAL CARTILAGES REPAIRED BY BONE. NATURAL SIZE.

A few spicules of bone are visible on the cartilages at a distance from the repaired fracture. A certain amount of movement obtained between the portions of cartilage and the interposed bone.

So far as the origin of new fibrous tissue is concerned, it is certain that regeneration takes place by the proliferation of pre-existing connective-tissue cells in the part, and it is not improbable that some share in the process is taken by the large non-granular mononuclear leucocytes (hyaline cells) which migrate through the vessel-walls in inflammation. At the present day we are not inclined to allow that newly formed connective tissue has any other origin.

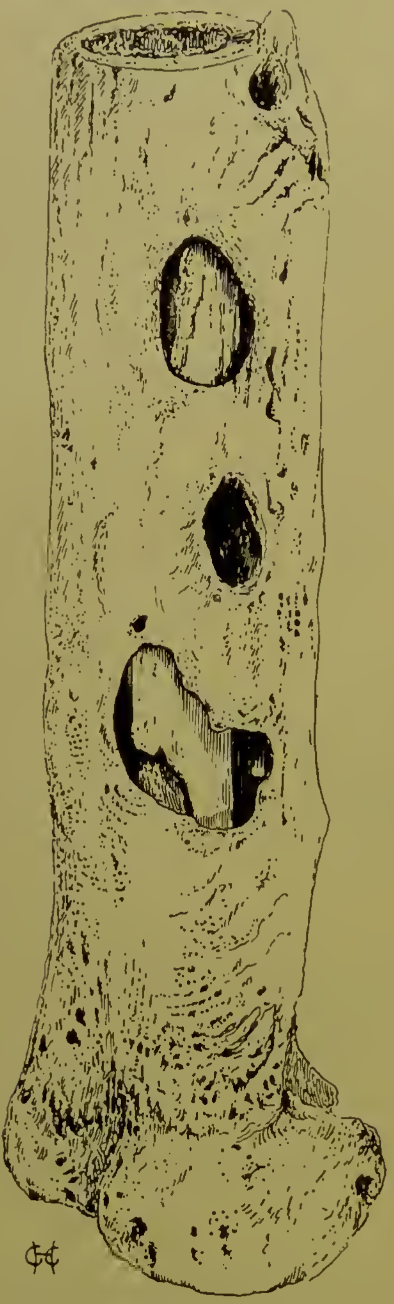


Fig. 15.—Hyperostosis around a Sequestrum of Femur. × $\frac{2}{3}$.

The shaft of the bone is rough and greatly thickened. Three cloacæ are seen, through two of which the sequestrum formed by the shaft of the old bone is visible.

Regeneration of bone is dependent upon the integrity of the periosteum; but given that this tissue is capable of exercising its function, there is hardly any limit to the degree to which regeneration of bone may take place. The entire shaft of the tibia may be removed subperiosteally and yet in course of time a perfectly new shaft will be formed. The method whereby regeneration of bone takes place is identical with that which brings about the normal growth of bone. That is to say, the periosteum becomes congested, the osteoblasts proliferate, new cancellous bone is formed either with or without the occurrence of an intervening stage of calcification, the cancellous spaces become narrowed by the deposition of concentric layers of new bone, and true Haversian canals are made. The newly formed bone corresponds very closely with normal bone, and, indeed, may be identical therewith, but as a rule it differs from normal bone in certain particulars. Thus it is often more voluminous, sometimes much denser, and generally far more irregular in its arrangement. These factors, however, are in large measure dependent upon what may be called accidental circumstances, such as movement, amount of bone for which regeneration is necessary, &c. The truth of this statement is nowhere better seen than in the case of the repair of fractures: the amount of new bone formed in the repair of a fractured rib, its relative porosity, and its irregularity, form a marked contrast to the small amount of dense and regularly disposed bone that is formed in the repair of a well-set simple fracture of a tibia which has been kept perfectly at rest while the regeneration of bone was proceeding. In all cases of very chronic inflammation the amount of redundant reparative material is considerable (fig. 15). Under no circumstances is regeneration of bone carried out through a preliminary cartilaginous stage.

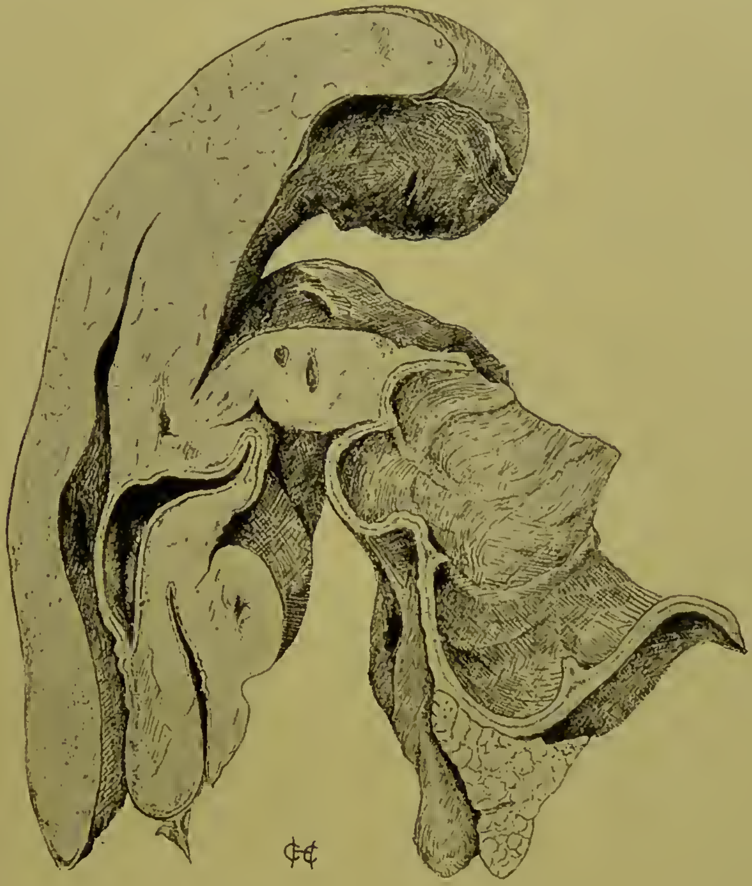


Fig. 16.—Chronic Inflammation of Omentum. × $\frac{3}{4}$.

From a case of ascites of long duration. The omentum (to the left of the figure) is enormously thickened and shortened. To the right of the figure is seen a portion of the stomach, with a portion of the pancreas beneath. In that part of the omentum nearest the stomach is the collapsed transverse colon cut across. The fundamental change consists in a great inflammatory overgrowth of fibrous tissue.

While we are dealing with this question it may be said that occasionally the repair of fibrous tissue by bone is seen. As a rule the condition stops short at the stage of calcification, but sometimes true ossification takes place. This occurs in the condition known as **myositis ossificans**, which is not, as its name would suggest, an ossification of the muscle, but rather an ossification taking place in the intermuscular planes of connective tissue. It is, however, a very rare condition. Calcification of a regenerated fibrous tissue, on the other hand, is by no means uncommon.

(3) **Muscle.**—It is doubtful whether true regeneration of muscle, striated or non-striated, ever occurs after its destruction. Undoubtedly both types of muscle can undergo increase in size, and if from any cause they have undergone a certain amount of disuse atrophy, they may, if the cause is removed, regenerate, and again reach their normal size. In this sense the growth of the unstriped muscle of the uterus at each successive pregnancy is a regenerative process, and the same is true of the recovery in size of the voluntary muscles that takes place after a long illness in bed. But it is not in this sense that the term 'regeneration' is employed, and if we use it in the same way as when we speak of the regeneration of epithelium, there is no doubt that regeneration of muscle is unknown, except in one instance to be mentioned immediately. When a portion of a muscle has been destroyed as the result of inflammation, its place is not filled by muscle, but by quite a different tissue, viz. fibrous tissue; repair takes place and not regeneration.

This fact is a very remarkable one, considering what we know concerning the growth of muscle, and particularly of unstriped muscle. It is a thoroughly inexplicable fact that one stimulus—an impregnated ovum—leads to increased growth of muscle fibres, while another stimulus—that connected with inflammation—leads to increased growth of connective tissue in one and the same organ. The same is true in the case of other hollow muscular organs, e.g. heart, intestine, urinary and gall bladders. Nor is the whole matter explained when it is acknowledged that increased work thrown upon a muscular organ leads to hypertrophy of its muscle, for in the case of the uterus no increased work is thrown upon the organ until parturition, and yet the uterine wall commences to increase in thickness directly the ovum reaches it. It is not the stimulus of the ovum alone which is efficacious, the ovum must be impregnated; an ovum probably passes through the cavity of the uterus at each menstrual period, but the organ does not hypertrophy at these times.

There is one condition, however, under which muscle may be fairly said to regenerate when it has been destroyed as the result of inflammation. When reparative tissue is being formed it is necessary that blood-vessels should also be formed to bring nutriment to the young tissue. At first, as will be seen later, these vessels are capillaries, but it often happens that after a long time the fully formed reparative tissue is found to contain perfect arteries and veins. Since these arteries and veins consist in part of unstriped muscle, it is clear that it must have been newly formed. There is reason to believe that it results from a proliferation of the muscular coats of the vessels from which the newly formed vessels themselves originate and with which they are still in continuity. The formation of the unstriped muscle, then, in this instance, is exactly comparable to the regeneration of epithelium which we have already considered.

(4) **Gland.**—Reference has already been made to the regeneration of the epithelium which lines the alveoli and the ducts of glands. We have now to consider the question as bearing upon the gland as a composite structure.

The question is naturally a complicated one owing to the diverse nature of glands. When one has to deal with simple glands such as the tubular glands of the uterus, we can apparently affirm with certainty that true regeneration occurs. Indeed, in the instance given the apparent regeneration of glands may proceed to excess, and the appearances of the uterine mucosa in a case of endometritis when seen under the microscope are those of hypertrophy and hyperplasia of the glandular elements. But here the appearances are deceptive, for it will be remembered that the uterine glands reach down into the muscular tissue of the uterine wall, so that when the endometrium is removed, whether at normal menstruation or as the result of operative interference, there is still left behind a portion of the gland from which a new gland—or, rather, a portion of a gland—can be renewed. But this is not the same thing as a regeneration of the gland *as a whole.* A very similar instance is seen in the case of a hair and the sac from which it springs; if the hair is cut, it grows again, but if the hair follicle is destroyed, it is doubtful if its place is ever filled by one of new formation.

In the case of larger masses of composite gland tissue such as the breast, there is not the slightest reason for believing that regeneration ever occurs. When a portion of such a gland as the breast has been destroyed in any way, its place is taken by reparative tissue, but never by newly formed gland tissue. In instances such as this, it is even doubtful whether the unaffected gland tissue surrounding a spot which has been destroyed, undergoes any hypertrophy or other compensatory change.

In the case of the liver and kidney the question of a possible regeneration has received especial attention. With regard to the liver it is generally accepted at the present day that true regeneration occurs, though how far the process takes place in actual life is uncertain. When a portion of the liver has been removed experimentally, the surrounding hepatic substance is seen, after a while, to be the seat of a considerable hypertrophy of the true liver cells, and at the same time many of the cells show the presence of karyokinetic figures. Hence we must allow that, besides hypertrophy, a hyperplasia takes place. The liver, however, in spite of its size, is a relatively simple gland considered in its purely anatomical aspect. It is little more than a congeries of spheroidal cells which have become polygonal from mutual pressure. The case is very different with the kidney, in which the glandular unit is a highly complicated structure. And though competent authorities have described the occurrence of karyokinetic figures in the remaining portions of a kidney of which one portion has been removed experimentally, the question as to whether true regeneration occurs after destruction of a part of this gland must be left a matter of doubt.

Sebaceous and sweat glands are not regenerated when once they have been removed or destroyed. This is well shown by their absence from ordinary scar tissue.

To sum up. Though we have ample evidence that true regeneration of the secreting epithelium of glands takes place, we have scanty evidence of a regeneration of gland substance. In the case of most glands, indeed, all the evidence goes to support the view that regeneration in them never occurs.

(5) **Blood-vessels.**—True regeneration occurs in the case of all kinds of blood-vessel, whether artery, vein, or capillary. Of the three classes, however, regeneration of capillaries is by far the most common. In fact, every kind of blood-vessel, whatever its ultimate type, commences its regeneration as a capillary, the distinctive features being added subsequently.

One of the best places for studying the new formation of capillaries is that part of the chorion in a fœtus of about two and a half or three months, which is afterwards to constitute the edge of the placenta. A section taken from this spot shows a number of solid masses of large cells which are in direct connection with pre-existing capillaries. At some point a spot will be found at which the lumen of the capillary is seen to be pushing its way into the solid mass of cells, and it is by the gradual hollowing out of the solid cylinders of cells that the new capillaries are formed. In many places the commencement of the process can be seen. This consists in a localised heaping up of cells at some point on the side of a capillary, the cells themselves being endothelial cells produced by proliferation of the endothelial cells at that spot in the capillary wall. The localised accumulation of endothelial cells increases in size and pushes its way among the surrounding structures in a direction more or less at right angles to the direction of the vessel from which it springs. The excavation of the solid cylinder of cells proceeds from the capillary on which it is seated, and there is always a certain length of solid cylinder, tapering in shape, in advance of the newly canalised, and now complete capillary. Sometimes one finds that there is a delicate partition between the newly canalised portion and the lumen of the capillary from which it springs, which prevents passage of the blood into the new capillary from the pre-existing vessel; but this partition does not long persist, and the blood finds its way into the new capillary and fills it. Other methods have been

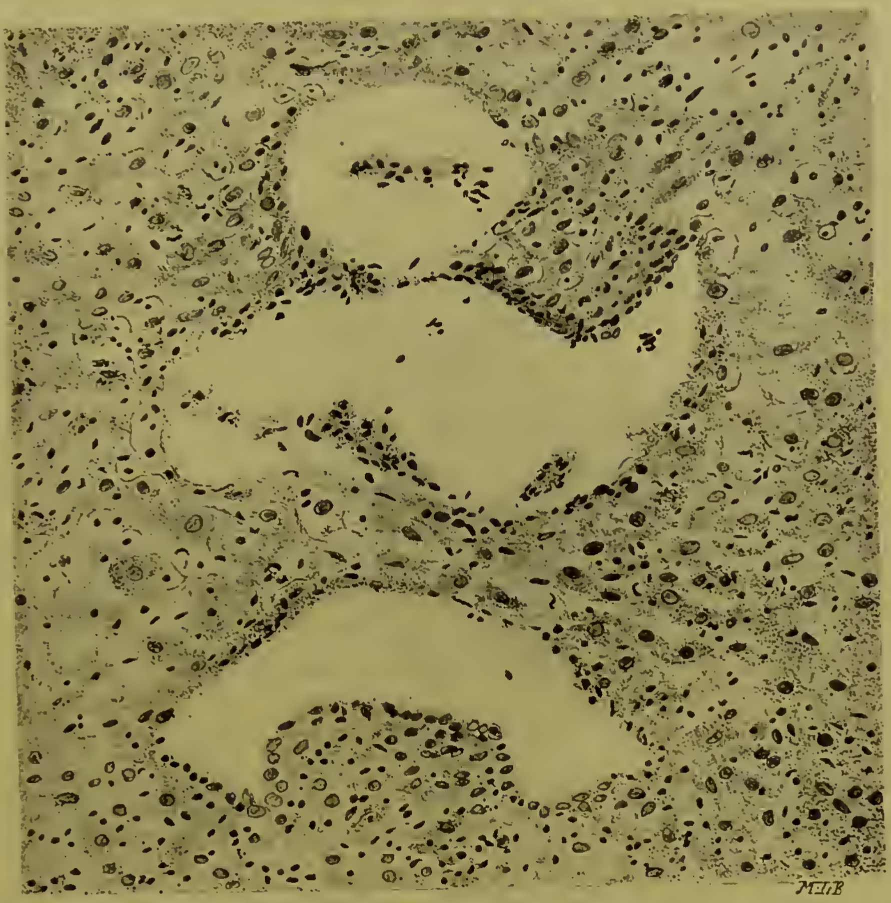


FIG. 17.—FORMATION OF NEW BLOOD-VESSELS. × 420.

A portion of the site of placental formation in a three months' abortion. Three blood spaces are seen, formation of the uppermost of which has just been completed by the meeting of the lateral buds. In the lowest vessel a large bud is seen to be projecting; it is covered with an endothelial-like layer of cells. The solid tissue around the new vessels shows many large decidual cells.

described for the formation of new capillaries, and there is no doubt that other methods exist, but their consideration need not delay us now, since they have only been observed in the embryo. The method which has been described above is the only one which obtains in extra-uterine life.

It often happens that solid cylinders arising from contiguous capillaries meet at their distal extremities. When this has occurred the two ends cohere, and canalisation proceeding in both, a channel is formed between the two original capillaries. This process is a very important one in connection with repair, as we shall see later. Where the repair is taking place in a wound or other situation denuded of an epithelial covering, the newly regenerated capillaries have a general direction at right angles to the raw surface, but they do not reach quite up to the free surface. At a little distance beneath it they bend into a direction parallel with the raw surface, and meeting with other newly formed capillaries which have taken a similar course, the ends of both cohere and thus a loop is formed very similar to the loops of Henle in the kidney. These loops are just visible with the naked eye, and as they reach close up to the surface of the wound and are full of blood, they appear as tiny red granules. From these characteristics the newly formed capillaries are often termed ‘granulation loops,’ and the entire reparative tissue of which they form so important a constituent part is called ‘granulation tissue.’

Arteries and veins are regenerated with far less frequency than capillaries, and even when formed are of small size. We are not fully acquainted with the processes of their regeneration. We know that they first exist as capillaries, and we believe that their muscular and elastic tunics are formed by an extension of the same coats from pre-existing vessels of the same type. It has been suggested that the muscular and elastic coats are formed from proliferated endothelial cells in the wall of the newly formed capillary, but it is probable that this view is erroneous.

(6) **Lymphatics.**—One of the most important characteristics of granulation tissue is that it contains no lymphatics. This fact has an important bearing, for since it is largely by the lymphatics that toxic substances formed by bacterial and other agencies in a wound gain access to the general circulation, it is clear that the absence of lymphatics in granulation tissue implies that when the healing of a wound has reached the point at which granulation tissue makes its appearance, the chances of septic absorption are greatly reduced.

Directly following from the statement that lymphatics are absent from granulation tissue there issues the statement that lymphatics are absent from scar tissue into which the granulation tissue ultimately becomes converted. Since the formation of scar tissue is, as we shall see, the commonest way in which destroyed tissue is replaced, it becomes difficult to see how a regeneration of lymphatics can take place at all. That extra-vascular lymph spaces must be formed is certain, but it does not appear that they are brought into connection with other than pre-existing lymphatic channels. It is quite possible that owing to the numbers of lymphatic channels in any part, and the freedom of their anastomosis, a necessity for regeneration of lymphatics does not arise.

Lymphatic glands and other masses of adenoid tissue, when once destroyed, are not regenerated, but the body does not suffer thereby, for loss at one point is compensated for by hypertrophy at another.

(7) **Nerve tissue.**—In considering the question of the regeneration of nervous tissue a very sharp line has to be drawn between the nerve cells and the nerves themselves. The neuroglia we may leave entirely on one side, for it is nothing more than a somewhat specialised form of connective tissue, and, as such, follows the laws that have already been laid down with reference to the regeneration of fibrous tissue.

There is no doubt that nerve cells, when once they have been destroyed, never regenerate. There is hardly a more certain fact in pathology than this. With regard to nerves themselves, meaning thereby the anatomical agglomerations of axis cylinders, the matter is different. There is, on the contrary, a considerable mass of evidence that regeneration of nerves sometimes takes place.

The evidence that a regeneration has taken place in a nerve that has been severed either experimentally or as the result of accident, consists in the restoration of function in the part which the nerve supplies. This function may, of course, concern either afferent or efferent nerves, and it may be here stated that no difference obtains between the two classes of nerves, excepting that a return of function is observed to take place sooner when an afferent nerve has been divided than when the lesion has involved an efferent trunk.

When a nerve has been divided the two cut ends separate to a greater or smaller degree, and the first stage in the regenerative process consists in restoring the anatomical continuity of the nerve. This act precedes the restoration of function by a long interval; in fact, such restoration of function may never occur. The cut ends of the nerve being situated in a part on which an irritant has acted, they become involved in a local inflammatory process, and with the surrounding tissues are subject to the sequels of inflammation. They thus become involved in the mass of scar tissue which, as we shall see later, repairs the wound. Between the two cut ends of the nerve, therefore, a mass of dense fibrous (scar) tissue is formed, and by this means the anatomical continuity of the nerve is restored.

It is at this point that the true regeneration of the nerve commences. If we reduce our conception of a nerve to its lowest limits, it consists of a ganglion cell in connection with which is a longer or shorter process—the axon or axis cylinder. Severed from its ganglion cell the axon infallibly dies. Myelin drops appear from the disintegration of the medullary sheath of Schwann, the cells within the neurilemma multiply, the axon disintegrates. These processes take place in the distal part of the divided nerve alone, but here they are complete. On the proximal side the axis cylinders and their enveloping sheaths undergo no alteration beyond the node of Ranvier immediately above the point to which the action of the irritant reaches, a very short distance if the wound which severed the nerve was aseptic. While the two ends of the (anatomical) nerve were being welded together by the mass of intervening scar tissue, the ends of the proximal portions of the divided axons were becoming bulbous, and ultimately dividing into a number of fine filaments. These filaments in course of time insinuate themselves among the fibrous-tissue bundles constituting the scar, traverse it, and, using the remaining elements of the distal end of the severed nerve as a scaffolding, travel in its track down to its ultimate branches. How they become converted into the appropriate nerve endings is unknown. Though many of the points of the entire process are still matters for discussion, the majority of authors agree that the fundamental steps in the process are those which have been set forth above. It is believed by some, however, that the distal portions of the axis cylinders are locally formed anew and are not merely prolongations of the proximal portions.

Before leaving the question of the regeneration of tissues it may be pointed out how all the processes resolve themselves into a growth of elements of the same nature as those which are to be regenerated; epithelium must proliferate for the regeneration of epithelium, one or other form of connective tissue for the regeneration of the connective tissues, axis cylinder for the regeneration of nerve. The separate systems of tissue remain separate throughout, and we never find fibrous-tissue cells forming an epithelium, or muscle cells a nerve. It is a different question as to whether different members of the same group can replace one another. We have already answered this question in the affirmative in the case of the connective-tissue group. In this group the degree of mutual interchangeability is considerable, but amongst the epithelia, though a certain amount of interchangeability exists, it is far less complete. The glandular type of epithelium seems to stand by itself; its place cannot be taken, seemingly, by either of the other two varieties. But a certain degree of interchangeability obtains between the squamous and the columnar types in that when a squamous epithelium becomes inverted and protected, its cells become less flattened, and when a mucous membrane covered by a columnar epithelium becomes exposed its cells in course of time become more or less flattened. Nevertheless, however similar in appearance to a true squamous epithelium a columnar epithelium may become, it never takes on the functions of an investing surface to such a degree that it conveys hair follicles or sweat glands. Nor does an epidermal surface when inverted take on any of the secreting functions of a columnar epithelium; it never forms mucus, for example. Neither does it entirely lose its function of conveying hair follicles and sweat glands; the activity of these constituents may be altered, but, in some degree, it is always present.

D.—REPAIR

From what has been said concerning the occurrence of regenerative processes in the body after destruction of its various constituent elements, it is clear that the effects of a wound would be disastrous were it not that some other process than regeneration can step in and mitigate, if not nullify, the effects of the injury. If the body can only in few instances regenerate, it can at least repair the injured tissues.

In an overwhelming preponderance of cases, repair consists in the new formation of fibrous tissue and fibrous tissue alone. This is the case whenever an injury or other irritant has caused destruction of any part in the depth of the tissues. Thus, when a muscle is ruptured, the two ends are joined together by a more or less regular and voluminous mass of firm fibrous tissue; when a portion of the spleen or the kidney dies because its circulation is cut off by some obstruction of its nutrient artery (infarct), the focus, after removal of the dead-tissue elements, is filled up by newly formed fibrous tissue; when the syphilitic virus, acting upon the liver, leads to a focus of inflammation and the destruction of hepatic cells, the place of the destroyed tissue is taken by newly formed fibrous tissue; when a portion of the central nervous system undergoes degeneration, its place, if the patient lives long enough, is filled by newly formed fibrous tissue, and so on. In the case of bone the same holds good, with the difference that whereas the ordinary connective-tissue corpuscle (fibroblast) forms around it a material which does not normally contain calcium salts, the osteoblast forms around it a tissue which does contain those elements. This only means, however, that the cells which are to form bone are derived from a special kind of matrix (the periosteum): if the fragments of a fractured bone are so far separated that the periosteum cannot bridge over the distance between them, junction between the ends is made by a new formation of fibrous tissue and not of bone. This is very well seen in the case of a fractured patella; if the case is left to itself the upper fragment, drawn up by the unrestrained action of the quadriceps femoris, is so far removed from the lower fragment, which is attached to the tibia, that the two ends never unite by bone but always by fibrous tissue. If, on the other hand, the case is treated by wiring the two fragments together, the distance between them is reduced to limits so small, that, *cæteris paribus*, union between them is firm and bony.

When one comes to consider conditions that have led to destruction of superficial parts, whether those parts are superficial from the external or the internal aspect of the body, the process is a little more complicated. For now we have to remember that the epithelium is a tissue which repairs itself by regeneration (the two terms being identical in signification in this instance). Here, therefore, repair is a combination of two processes instead of one. It may safely be said, however, that cases are excessively uncommon in which repair consists of more than two processes, of which one consists in the new formation of some one or other member of the connective-tissue group—usually white fibrous tissues—and the other consists in the regeneration of an investing epithelium of the simplest type.

We shall most easily gain an understanding of the unity of repair by considering in short detail some specific examples. For this purpose, too, it will be advisable to choose examples that are apparently widely different, such as the repair (1) of a clean-cut wound reaching down to, but not involving, the subjacent muscle; (2) of a simple fracture of bone; (3) of a typhoid ulcer; (4) of an abscess connected with bone, and (5) of a serous surface such as the pleura which has been damaged by inflammation. Unlike as these conditions are in their clinical aspects, in their causation, and in their course, it will appear that the processes by which repair is brought about in all the cases are identical in essence.

(1) **Repair of a clean-cut wound.**—When a cut is made into the tissues the effects that are produced vary enormously according to the depth of the wound, the sharpness of the instrument which causes it, and, above all, according as the instrument is aseptic or septic. These differences, however, are differences of degree rather than of kind. So long as the wound involves the true skin a certain amount of blood is poured out, a certain number of cells are damaged or killed. We will suppose that the wound has reached well into the subcutaneous tissue and that it has been untended after its production.

As a result of the normal tonus of the tissues, when an incision has been made into them the wound gapes, and between its edges there collects some of the blood which flows. At length, for reasons that will be considered along with the subject of thrombosis (Section VI), the ends of the divided vessels are closed up, and coagulation occurs in the blood that still remains between the lips of the wound. This coagulum contracts, and because the fibrin of which the clot so largely consists is closely adherent to the lips of the wound, it draws these lips together. At the same time the irritant action of the injury, combined with the subordinate irritants constituted by the dead-tissue cells, the blood clot, &c., leads to the appearance of the phenomena of inflammation. Exudation of fluid occurs and leucocytes emigrate through the vessel-walls. Chiefly as the result of the action of the phagocytic leucocytes, the red blood corpuscles in the blood clot are broken up and removed, so that the clot, which was at first red, ultimately becomes greyish-white. Dead and dying tissue elements are also removed by the same agency, while such bacteria as may have gained access to the wound are englobed by the leucocytes after they have been exposed to the bactericidal action of the blood serum. The way is now paved for the occurrence of repair.

The action of the irritant which, close to the edges of the wound, led to inflammation, at some varying distance from the edges, ceased to have an irritating effect, but became stimulating. That is to say, instead of leading to degenerative processes it leads to proliferation. The cells upon which this stimulating action is exerted are the connective-tissue cells (and, perhaps, the mononuclear leucocytes), and they form a number of fibroblasts. At the same time the stimulus acts upon the cells of the capillary blood-vessels, and they commence to bud and form new blood-vessels. Both of these processes take place at some little distance from the raw surfaces of the wound, and the direction taken by the newly formed blood-vessels is one at right angles to the raw surface. In course of time the regenerated capillaries reach the surface, and, using the fibrin of the blood clot which lies between the surfaces of the wound as a scaffolding, traverse the altered blood clot, and, meeting with similar newly formed capillaries from the other side, completely bridge across the space which formerly existed between the two lips of the wound.

While this process of vascularisation has been going on the fibroblasts have not been idle. They have ranged themselves alongside the new capillaries, deriving nutriment from the contained blood, and at the same time affording support to the delicate channels by investing themselves with that material—fibrous tissue—which it is their function to make. In course of time the entire space between the cut surfaces of the wound is filled by an intensely vascular, young, and therefore highly cellular, connective tissue; in a word, with granulation tissue. The amount of fibrous tissue increases until the newly formed tissue becomes firmer and denser than the surrounding tissues. It is then known as a **scar** or **cicatrix**.

While these changes have been going on the epithelium has been holding itself in readiness to complete the process. So soon as the irritant action on the surface has abated sufficiently, the epithelial cells begin to divide, division taking place in two directions. Close by the cut edge division is at right angles to the superficial surface, and by this means the growing epithelium creeps over the surface of the newly formed fibrous tissue until at last the entire raw surface is covered with a thin layer of epithelium. As this is proceeding, division of the epithelial cells is taking place in the normal plane—parallel to the cutaneous surface—and in this way the epidermal layers covering the scar attain a certain thickness. They are never, however, as thick over a scar as they are in the neighbouring normal parts.

Owing to its extreme vascularity, a recent scar is redder in colour than the surrounding skin and projects somewhat above the surface. But it is a normal characteristic of fibrous tissue to contract, and as a result a large number of the blood-vessels in a young scar become obliterated in course of time. This gives rise to the depressed, dead-white appearance of a cicatrix with which we are so familiar.

(2) **Repair of a simple fracture of bone.**—The term 'simple' as applied to fractures of bone has a special signification, and is contrasted with 'compound.' By a simple fracture is meant one which is not in communication with the open air, and which is, in consequence, aseptic. A compound fracture, on the other hand, is one which is in communication with the open air, owing to laceration of the skin; it is commonly, though not invariably, septic. We shall see later in what points the two varieties of fracture differ pathologically, but since the repair of a simple fracture is somewhat less complicated than the repair of one which is compound, it will serve our present purpose better to confine our attention to the simple variety and to defer consideration of repair of a compound fracture until we come to discuss the repair of an abscess connected with bone.

When a bone has been fractured subcutaneously a certain amount of damage has been done to the soft parts in its immediate neighbourhood; portions of muscle and of tendon have been torn, blood-vessels have been lacerated and have led to extravasation of blood, and the periosteum has probably been torn or at least has suffered injury. As a result, the fractured ends of the bone lie in the midst of a mass consisting of injured tissues and blood clot, and this mass not only envelopes the ends of the bone on their external aspects, but also is present within the medullary cavity, if the bone under consideration is a long bone. To this mass are soon added the products of that inflammation which arises as the result of the irritant action of the injury and the subordinate irritants to which the injury gives rise, and the coagulation of the entire mass tends to restrict the movement of the ends of the fragments. The condition is now exactly comparable to the condition found in the case of an incised wound.

The extravasated red blood corpuscles now begin to disintegrate, and their fragments are removed by the phagocytic cells reaching the spot in the course of the inflammation. At the same time new capillary blood-vessels are formed and penetrate into the mass, aiding the removal of such materials as are useless and carrying nutriment for the cells which are to repair the fracture.

During the time that these processes have been going on the periosteum has been subjected to irritation at a point contiguous to the fracture, and to stimulation further off. A certain portion of it therefore dies, but owing to the simple nature of the fracture and the consequent absence of bacteria, the amount of periosteum which dies is small. That portion which is subjected to stimulation becomes congested and the osteogenetic layer shows signs of active proliferation of its component cells. The same is true in the case of the endosteum.

Within the shaft and outside the ends of the bone, therefore, an active proliferation of cells is taking place, and these, applying themselves to the sides of the newly formed capillaries, penetrate along with them into the mass of material in which the ends of the fractured bone are placed. But these proliferated cells have arisen from tissues the normal function of which is to form bone, and they fulfil their inherited function. At first they deposit calcium salts in the interstitial substance which they form, and since they are arranged around the blood-vessels, the mass of material which surrounded the fractured ends of the bone becomes converted into a calcareous mass of irregular constitution in the meshwork of which numbers of capillaries ramify. This material is known as **callus**, and it invests the broken ends of the bone with a relatively firm material which keeps them at rest until the process of repair has been fully completed.

The mass of callus which lies between the broken ends of the bone has received the attribute *definitive* to distinguish it from the masses which lie within the shaft and outside the ends of the bone, and which are spoken of as *provisional.* It is the definitive callus by means of which the ultimate repair of the bone is brought about; the provisional callus is only of temporary importance and disappears in course of time.

The way has now been prepared for the occurrence of true ossification. This process takes place to some extent throughout the entire mass of callus, but it is only in the case of the definitive callus that it reaches a high degree of perfection; here, however, a true bone is produced which is of extreme density.

Repair of the bone is now complete, but just as certain changes go on in a young scar which essentially consist in the removal of redundant fibrous tissue, so in the case of the newly repaired bone. At first the central canal of the bone is obliterated by the endosteal callus, and there is an excess of callus on the outside, but in course of time the medullary canal becomes re-established and the excess of callus is removed. In a favourable case the entire process is carried out so effectively that it ultimately becomes almost impossible to distinguish that the bone has been fractured at all. That there will be differences in the amount of provisional callus, in the length of time before repair is complete, in the positions of the ends of the bone to one another, according to the degree of injury, whether they are kept at rest or are constantly moving, the age and general recuperative power of the patient, and so on, is self-evident, and these considerations need not detain us now.

(3) **Repair of a typhoid ulcer.**—As the result of the action of the typhoid bacilli and the toxin which they produce, aided probably by the action of other bacteria in the intestines and their products, the Peyer's patches in the small intestine and the solitary follicles in the small and large intestines become the seats of inflammation. This inflammation shows itself by the regular phenomena, the congestion appearing in the blood-vessels running beneath the serous coat, the exudation of fluid and the migration of leucocytes showing themselves by a swelling of the Peyerian patches and their projection beyond the common level of the intestinal mucous membrane. The action of the various irritants is so intense that the Peyer's patch or the solitary follicle dies in mass. The dead mass now begins to act as an irritant, and being adherent by continuity of tissue to the subjacent parts, its action persists. Pathological sequels of inflammation are therefore produced, the chief of which is the formation of pus at the edge of the dead mass of adenoid tissue where phagocytic cells are occupied in severing the connection of the dead mass with the living. Ultimately this separation is effected, and the dead mass of adenoid tissue is cast into the lumen of the intestine as a slough. The typhoid ulcer is now constituted of which we are about to consider the repair.

When the slough has been removed, a fertile source of irritation disappears, and the floor of the ulcer, though exposed to the irritating action of the intestinal contents which flow over it, protects the deeper tissues. Beneath the intestinal surface of the ulcer, granulation tissue is formed—indeed it is formed before the separation of the slough—and this granulation tissue proceeds, if the case be favourable, to the formation of fibrous tissue in the ordinary way. Over the surface of the newly formed fibrous tissue an investing layer of epithelium is laid by proliferation of the epithelium surrounding the ulcer, and the cicatrix is complete.

This is the first occasion on which the formation of granulation tissue has been said to have an important share in the production of the repair, and it will be well if we delay for a short time to consider more in detail the exact constitution of this most important variety of tissue.

Granulation tissue.—In order to obtain a good specimen of granulation tissue we must take a portion of the tissue which is present in the neighbourhood of a focus of chronic inflammation. This is not because granulation tissue is only formed in cases of chronic inflammation, but because it is only then formed in sufficient amount to be suitable for microscopical examination. In all forms of repair it is present, but in the absence of pathological sequels of inflammation—in other words, when the irritant has been an aseptic one—the amount of granulation tissue that is necessary to fully repair the injury is so small that it is only with difficulty that its presence can be recognised at all.

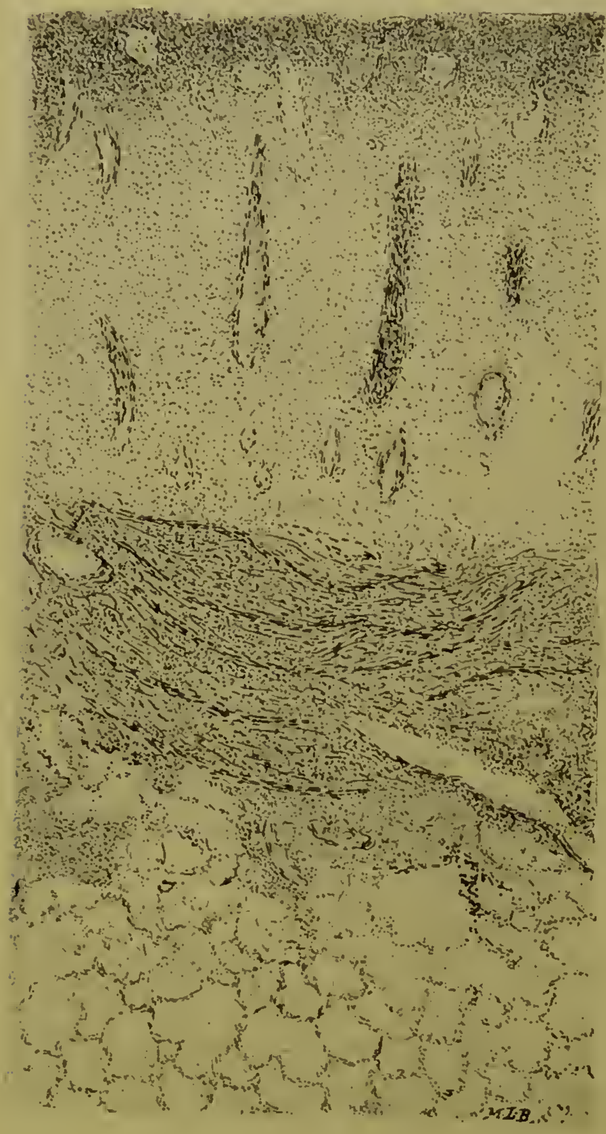


Fig. 18.—Section of Granulating Ulcer. × 18.

(1) At the free surface is the (darker) layer consisting principally of leucocytes, which will break down into pus; it contains the cross sections of a few capillary loops. (2) Below is a (paler) layer with few leucocytes and new capillary vessels running at right angles to the free surface. (3) Below these is a layer of young but well-formed fibrous tissue, having a general direction parallel to that of the free surface. (4) Finally is a portion of normal subcutaneous areolar tissue.

Taking, then, the floor of a chronic but healing ulcer as an example, and making a microscopical section in a direction at right angles to the raw surface, we shall be able to distinguish the following layers. On the surface is an accumulation of small round cells—pus cells—which cohere to a very slight extent owing to the presence of a small amount of fibrin. Beneath this layer is one in which the fibrinous network is much more distinct and the number of small round cells is much smaller; as a result this layer appears of looser texture, and, containing fewer elements which stain deeply, it affords a great contrast in colour, when viewed by the naked eye, to the more deeply stained layers above and below it. Reaching for some distance into this layer one can see with the naked eye a number of narrow deeply stained lines which run in a direction at right angles to the surface of the ulcer; these lines the microscope shows to be tiny blood-vessels—the granulation loops—the walls of which consist of a single layer of endothelial cells supported on the outside by a layer of young connective-tissue cells and a minute amount of fibrous tissue which these cells have formed. Between these granulation loops there is, of course, a fibrinous network with a few leucocytes. Still deeper is a fairly broad layer which consists of granulation blood-vessels clothed with a more definite layer of young fibrous tissue, and the amount of this tissue arranged parallel with the new capillaries increases as one passes from the more superficial to the deeper parts of the section. At the same time the amount of fibrin and the number of the small round cells (leucocytes) diminish.

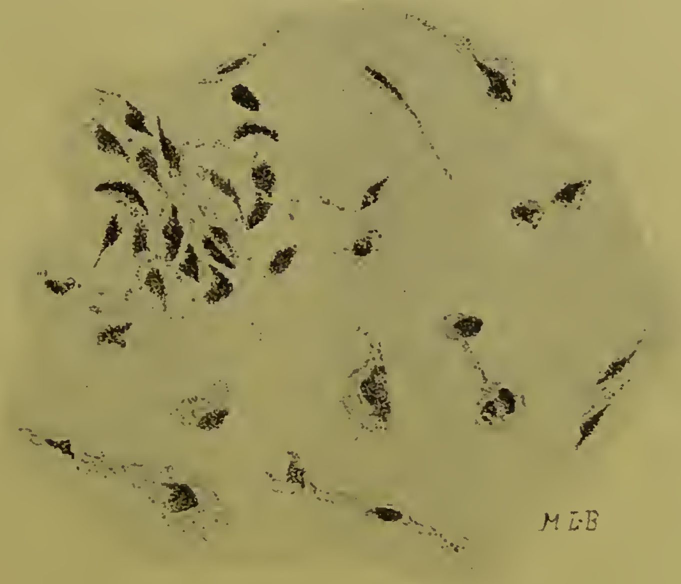


Fig. 19.—Granulation Tissue Cells. × 180.

From a scraping stained with picrocarmine and mounted in Farrant's medium. The cells are irregular in shape, but for the most part vary between round and fusiform. The nuclei are similar in shape.

Beneath the layers we have hitherto considered, we come to a layer of varying thickness of which the characters are in marked contrast to the others. For its elements, instead of having a general direction at right angles to the raw surface of the wound, have a direction parallel with that surface. This layer consists, like the one above it, of newly formed connective tissue which is highly vascularised; but though it is largely composed of cells, the cellular element is much less, and the fibrous character is much more evident. At the same time the connective-tissue fibrils are arranged in a series of planes at right angles to the capillaries and not parallel with them. It is this arrangement of the connective-tissue fibrils which is the important factor in the subsequent conversion of a young prominent and red cicatrix into an old depressed and white one, for the gradual contraction of the connective tissue placed in planes at right angles to the direction of the blood-vessels ultimately constricts and obliterates them. Finally, through a series of layers of fibrous tissue of increasing density and of longer formation, one reaches to the normal tissues beneath.

It must not be supposed that the layers that have been described above are sharply defined from one another. Such is not the case, although a section of a healing ulcer when viewed by the naked eye easily allows the existence of the separate layers to be recognised. Nor do we always find that granulation tissue consists of layers arranged in so orderly a fashion. In many cases we lose sight of the more delicate fibrous tissue and the fibrin, and the section consists of a more or less irregularly arranged young fibrous tissue in which there is an unusual number of capillary blood-vessels, and perhaps here and there a few leucocytes. Tissue of this kind is often of cartilaginous hardness and of considerable extent.

Giant cells.—A variety of cell which has hitherto only been mentioned—the giant cell—is not infrequently met with in granulation tissue (cf. figs. 20 and 25). This cell has microscopical characters which render it a very conspicuous object. It is many times the size of an ordinary cell, often being five or six times and sometimes being as much as twenty times the size of a leucocyte. But not only does it differ from most cells in its magnitude, it also differs in the fact that it always has a considerable number of nuclei; frequently ten may be counted and not uncommonly a hundred. The cell usually consists of a considerable amount of protoplasm, but the protoplasm is undifferentiated, so that a giant cell consists in its typical form of a large mass of protoplasm containing numerous nuclei. Sometimes the nuclei are irregularly scattered through the cell, sometimes they are crowded together to so great an extent that it is difficult to recognise the intervening protoplasm, and sometimes the nuclei are collected together at one pole of the cell while the remainder of the cell protoplasm is destitute of nuclei.

It is customary to use the term 'giant cell' for the appearance seen in one microscopical section, but as a matter of fact this usage is wrong. For we only see in a single section a small part of a giant cell. If we make serial sections of a portion of tissue in which giant cells are present, we shall find that the length of the cell is often very considerable, 40–50μ, for example, a length equal to six or eight times the diameter of a red blood corpuscle.

The exact meaning of the presence of giant cells in a mass of granulation tissue is uncertain, beyond the fact that they may probably be taken as a sign of chronicity. Neither is their origin certain. They have been regarded as the result of an imperfect cell division, the nuclei dividing in the ordinary fashion but not the cell protoplasm, and this view is probably the correct one; under these circumstances the giant cell would be regarded as a more or less degenerate form of cell. But it has also been held that they are formed by a fusion of cells, the nuclei remaining distinct but the protoplasm fusing into a general undifferentiated mass. Yet a third explanation has been put forward, viz. that giant cells are artefacts, and are only transverse sections of lymphatic or capillary blood-vessels, the contents of which have coagulated *in situ.* This would account for the granular and undifferentiated appearance of the protoplasm. And if we assume that there is a general or a local proliferation of the endothelial cells lining the vessel, an explanation is afforded for the entire appearance of a giant cell.

The function of giant cells is uncertain, but there is no doubt that in many instances they are phagocytic. In the case of bone, when inflammation occurs, a large number of giant cells is to be found in the immediate neighbourhood of any bone that is to be removed. The cells are placed in direct apposition with the trabeculæ of bone and are identical in appearance and function with the osteoclasts that are found in a normal growing bone. In both instances, too, their function is the same, viz. the removal of bone.

Although they are not by any means confined thereto, giant cells are found with exceptional frequency in the chronic inflammation of tuberculosis. So much so, indeed, that if we find giant cells in a microscopic section of a mass of granulation tissue, the suspicion immediately arises that we are dealing with an example of that specific inflammation. The arrangement of the nuclei in the giant cells of tuberculosis is somewhat peculiar;

there is a tendency for them to be collected at one end of the cell, and often to be arranged circumferentially in that position. It must not, however, be supposed that such an arrangement is more than a common one; it is suggestive but not conclusive.

(4) **Repair of an abscess connected with bone.**—Here we have to do with a septic process and one, moreover, which has been accompanied by the necrosis of a certain portion of the bone. As a rule an abscess of bone is associated with the formation of a sequestrum, so that the only differences between a typhoid ulcer and an abscess connected with bone are that in the case of a typhoid ulcer the dead material, the slough, is soft and the pus flows away as soon as it is formed, whereas in the case of the abscess connected with bone the sequestrum is osseous and the pus collects locally. These two features of the case where bone is concerned lend to it a remarkable chronicity, for the abscess has to point and the sequestrum has to be removed before repair can take place. Of these two features the osseous character of the dead material is by far the more important, and the actual size of the sequestrum practically determines the length of time that shall elapse before repair can take place, or at least before it can be completed. The reasons for this are three: in the first place, the calcareous elements of the sequestrum must be dissolved and removed before the proteid substratum can be dealt with by the phagocytes; secondly, the sinus by means of which the pus escapes is not sufficiently large to admit of the passage of more than a very small particle of separated bone; and thirdly, such repair as does take place is often a direct hindrance to the removal of the sequestrum.

In the separation of a necrosed portion of bone from the living portion of the same bone with which it is at first in organic continuity, it is of course not necessary that a solution of the calcareous elements of the entire mass should be brought about. In point of fact this process only occurs at the junction of the dead with the living, as in the case of the separation of the typhoid or any other slough. Hence a sequestrum consists of dense bone if it is of any size, and only the edges and the under surface are irregular and spiculated.

It has been insisted upon in a previous place that the degenerative action of an irritant must at some point become converted into the proliferative action of a stimulus. It is just for this reason that the processes of repair are at times distinctly disadvantageous to the proper repair of bone. For the stimulative action is brought to bear upon the cells of the periosteum, and these, fulfilling their normal function, form new bone. The principal factor in deciding where this new bone shall be formed is the position of living periosteum. At first, living periosteum is only found beyond the area represented by the portion of dead bone, and it is here that the new formation of bone commences to manifest itself. But not only does the stimulus lead the periosteum to form bone, it also leads the periosteum to regenerate a bone-forming membrane of a similar nature to itself. This newly formed periosteum may apply itself over the region at which the periosteum has been destroyed, viz. over the dead bone. Under these circumstances it commences to form new bone, with the result that when the necrosed portion has become separated from the living, the sequestrum finds its way to the exterior barred by a more or less extensive layer of new bone. This case of newly formed bone is often called an **involucrum**, and it is clear that the chances for a removal of the sequestrum without the aid of surgery are very small. It is true that such pus as is formed around the sequestrum finds its way to the exterior through openings in the newly formed bone (**cloacæ**), but these openings are valueless for the removal of any but a very small sequestrum. (Cf. fig. 15.)

Full repair, then, in the case of an abscess connected with bone cannot take place until all the dead material has been removed and all irritant action has ceased. When these criteria have been attained, the process of repair takes place in the same way as occurs in the repair of a simple aseptic fracture. That is to say, the periosteum forms new bone until the lacuna has been filled up. At first the new bone is present in excessive amount, and is very irregular in its arrangement. Subsequently a large portion of the excess is removed, the irregularities are rounded off, and the bone becomes denser than the surrounding bone; often, indeed, it is so dense that the condition of **sclerosis** is said to have occurred. While these processes have been going on in connection with the bone, the granulating surfaces constituting the wall of the sinus come into apposition, and, no longer being irritated by the passage over them of pus, the space between them becomes bridged over by newly formed fibrous tissue. Finally the orifice of the sinus becomes closed and covered by a layer of new epidermal cells, and repair is complete. Such a fortunate termination is, however, excessively rare without the aid of surgery, and cases of such a kind as we have supposed, untreated, drag on for years. Under proper surgical treatment, and if dealt with boldly and thoroughly at an early stage of their history, they proceed to recovery far less infrequently than might be supposed from a consideration of the difficulties that lie in the way of a natural repair.

(5) **Repair of an inflamed pleura.**—Taking a very common example, we will suppose that the cause of the pleurisy has been the extension to the serous surface of an inflammatory process starting in the lung. As a consequence of the inflammation the capillary blood-vessels of the visceral pleura, which are very numerous, become congested, and allow of the exudation of a considerable amount of fluid and of the migration of a variable (but generally small) number of leucocytes. The exudation passes into the pleural cavity, and there frequently undergoes coagulation. This coagulation leads to the deposition of a layer of fibrin upon the serous membrane, both visceral and parietal, and the two surfaces become loosely glued together. The subsequent history depends upon whether the endothelial covering of the pleura has been destroyed in the process or not.

In not a small number of cases we find on careful examination of the serous surface with the deposited fibrin, that the layer of fibrin can be stripped off leaving a fairly normal surface beneath. When this is the case, it is probable, judging from the analogy of the peritoneum, that the fibrin forms loose flakes which float in the exudation and are subsequently removed. Under these circumstances the process which takes place is clearly one of resolution, and we should expect that the pleura should return to a perfectly normal condition. It is difficult to assert that this is actually the case, but it is certain that we never see a case of lobar pneumonia in the post-mortem room in which the pleura over the consolidated portion of lung is not covered by a thin layer of fibrin, and it is equally certain that when uncomplicated recovery takes place from an attack of pneumonia the lung and the pleura give no evidence of their previous inflammatory condition.

On the other hand, when the endothelium has been destroyed the subsequent history of the pleurisy is one of repair and not of resolution. By the removal of their covering, two raw surfaces of pleura are opposed to one another, and the changes which supervene are exactly similar to those which we have seen to take place between two surfaces of an incised wound. That is to say, newly formed capillary blood-vessels derived from the pre-existing capillaries in each of the two pleural layers, penetrate into the intervening mass of fibrin and afford nutriment and support to newly proliferated fibroblasts derived from the same regions. The pleural space, therefore, which was at first filled with fibrin, becomes gradually filled with a mass of granulation tissue, young blood-vessels passing between the two pleural surfaces. The fibroblasts to which these capillaries give support form fibrous tissue in the ordinary way, and consequently the two layers of the pleura become mutually adherent by an intervening fibrous tissue which increases in density as time goes on, and which is in reality nothing more than scar tissue.

The extent to which adhesion takes place between the two layers of the pleura varies, of course, in different cases; in one it may be that there are formed only one or two delicate bands of fibrous tissue passing between the two pleural layers, and scarcely interfering at all with their gliding movement upon one another, and in a second case it may happen that the entire pleural cavity is obliterated by a mass of fibrous tissue nearly an inch in thickness and of cartilaginous hardness. Nevertheless, the processes in the two cases differ in extent only, and not one whit in kind. When the fibrous adhesions are as universal and extensive as in the instance last mentioned, it is not uncommon for calcium salts to be deposited in them subsequently. But this is only an example of the fact that calcareous deposition is especially liable to occur in tissues of a very low vitality and ill supplied with blood-vessels. Pleural adhesions offer no peculiarity in this respect; an adherent pericardium may become converted into a calcareous case for the heart, and the fibrous capsule formed around any aseptic foreign body situated in the midst of the tissues is very likely to undergo the same modification.

We have now considered the various examples of repair which were chosen at random to illustrate the processes at work under the most different conditions, and it is clear that in one and all of them repair is brought about by the formation of granulation tissue, which subsequently becomes converted into either ordinary fibrous tissue or bone, according as the connective-tissue elements upon which the stimulative action is exerted are those which normally form fibrous tissue or normally form bone. We have seen that the only difference between the repair of a bone and the repair of a soft tissue depends upon the fact that the presence of calcium salts in the case of bone protracts the duration of the case. We have seen that, though the amount of granulation tissue which is formed when the process is aseptic is far smaller than when the process is septic, yet repair takes place in both cases by the formation of the same granulation tissue which subsequently becomes converted into dense scar tissue. We cannot but conclude that, in spite of minor differences, in spite of the slightly different degrees in which true regeneration enters into the process in different cases, there is one single scheme, and one only, upon which repair is carried out.

SECTION IV

THE ANATOMICAL AND HISTOLOGICAL APPEARANCES OF CERTAIN SPECIFIC INFLAMMATIONS

In the case of certain specific inflammations the microscopic lesion produced is often so characteristic that it has long been customary to accord them a separate description in works on pathological anatomy. These specific inflammations are all characterised by the fact that the lesion which they produce is built up on the type of granulation tissue, and since they are all infective in the sense that the micro-organism which causes them has been isolated and proved to stand in a causal relation with the lesion, or in the sense that they are clinically infective, they were long classed together in one group, and known under the name of the 'infective granulomata.' Certain authors, indeed, still make use of the term, but it is probably destined to disappear, since we now know that the formation of granulation tissue is a characteristic of every kind of repair, while recognition of the fact that a vast majority of inflammatory lesions are infective in the sense that they are the result of the action of a bacterial irritant, deprives the term 'infective granuloma' of any special significance which it at one time possessed. The members of the group are tuberculosis, lupus, syphilis, actinomycosis, glanders, and leprosy. A few words will be said upon the incidence of each of these, but it must at the outset be recognised that microscopical examination alone is generally insufficient for making a diagnosis between them.

TUBERCULOSIS AND LUPUS

The typical lesion in the case of tuberculosis is a mass of a somewhat specialised variety of granulation tissue, so small that it has been compared to a millet seed, and for that reason has been termed a 'miliary tubercle.' In a schematic form the miliary tubercle consists of a giant cell in the centre, which is surrounded by a zone of elongated cells with a somewhat faintly staining nucleus, and this, again, is surrounded by a zone of small round cells which have but little cytoplasm, but contain a deeply staining nucleus which is commonly round in shape. These latter are often called **lymphoid cells** to distinguish them from the cells of the layer immediately internal to them, which are commonly termed **epithelioid cells**. The lymphoid cells are apparently identical with lymphocytes, and the epithelioid cells cannot be distinguished from young connective-tissue cells or fibroblasts. We have in a tubercle, therefore, the same elements that we meet with in any case of chronic inflammation, though it must be granted that they are arranged in more orderly fashion,

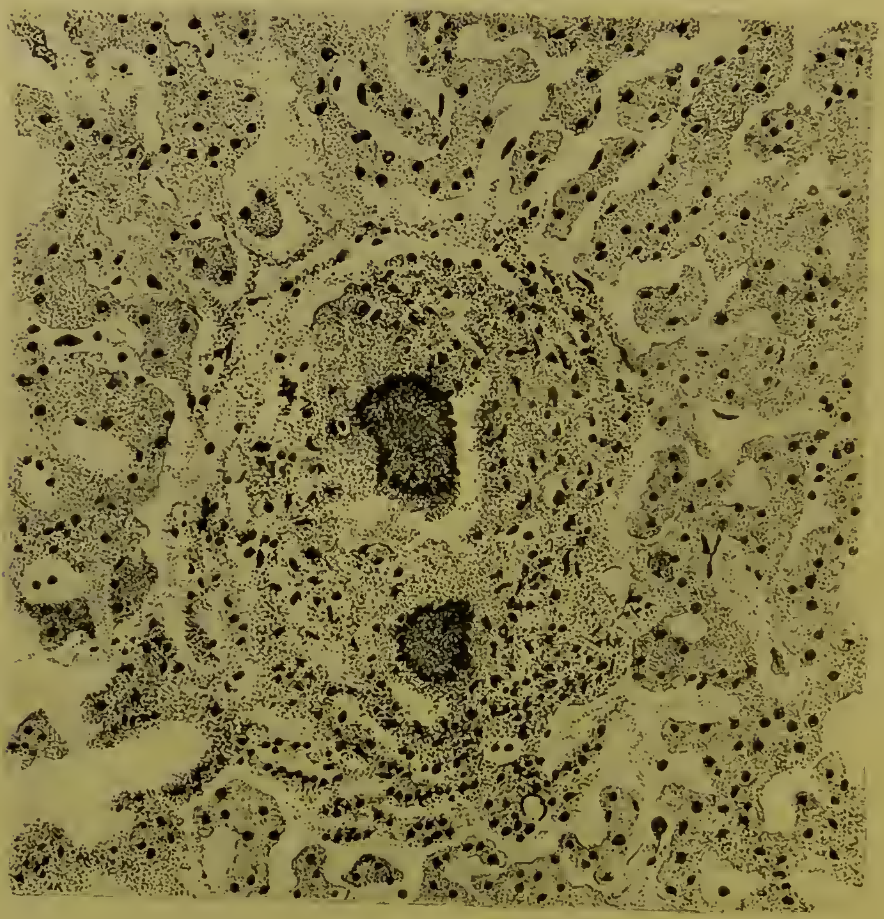


Fig. 20.—A Miliary Tubercle. × 420.

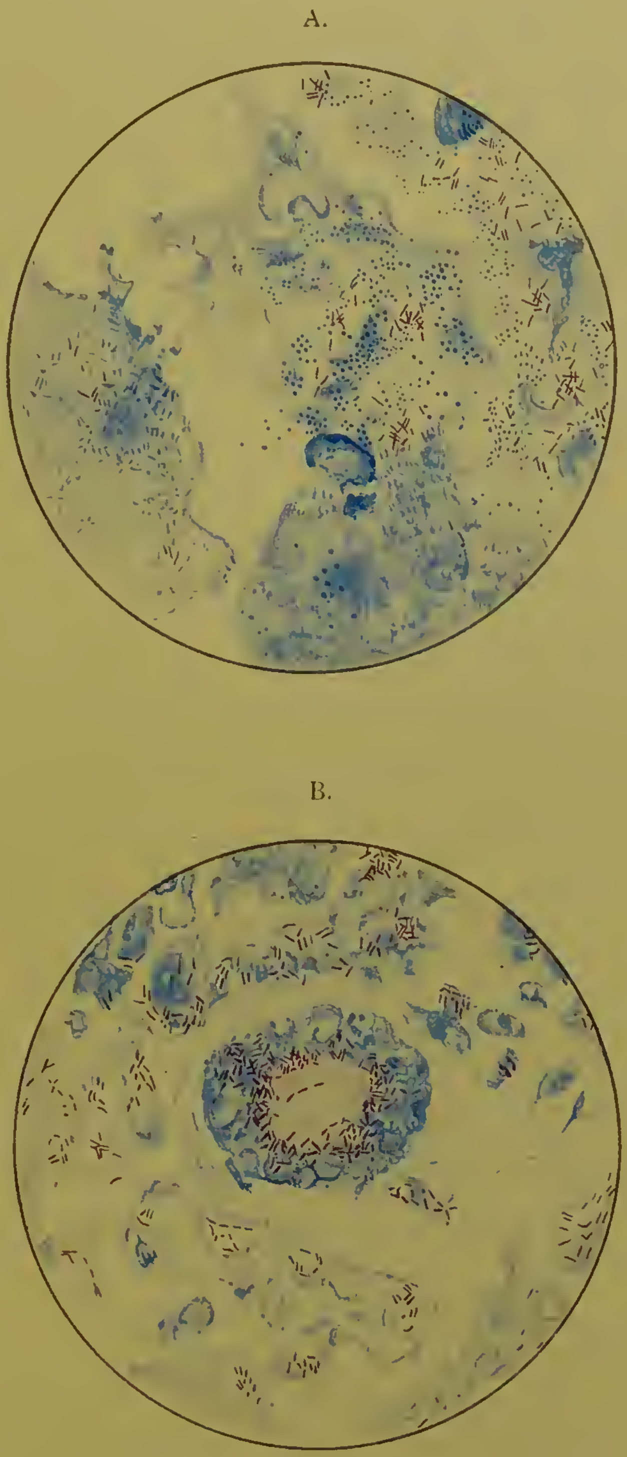
From the liver of a child. In the centre of the tubercle are two multinucleated giant cells, around which are arranged irregularly the elongated nuclei of endothelioid cells and the rounded, smaller, nuclei of leucocytes. The granular material between the nuclei of the tubercle represents the bodies of the cells altered by hardening reagents, &c. The hepatic capillaries are widely distended. Cf. fig. 25.

PLATE V

Fig. A.—Urinary deposit showing tubercle bacilli. Numerous other bacteria of various kinds are also present, but are stained blue. Cover-slip film from centrifugalised urinary deposit in a case of renal tuberculosis. Carbol-fuchsin, 1–3 alcoholic nitric acid, methylene blue, Canada balsam. Magnified 800 diameters.

Fig. B.—Section of lung of ox, showing tubercle bacilli in a giant cell. The bacilli are thickly collected in the periphery of the cell, the centre of which has undergone caseation. The bacilli in bovine tuberculosis are slightly shorter and thicker than in the human variety. paraffin section, carbol-fuchsin, 1–4 hydrochloric acid, methylene blue, Canada balsam. Magnified 800 diameters.

Plate V.



Tuberculosis.

and that there is, in the tubercle, an absence of those blood-vessels which we have seen to be a characteristic of granulation tissue. The absence of blood-vessels in all the manifestations of tuberculosis is one of the most remarkable features of the disease, and is accountable for the occurrence of that degenerative change—caseation—which is extremely common in tuberculosis, though it cannot be said to be characteristic of the disease. Of the fact that there is a complete absence of blood-vessels in a tubercle there can be no doubt, but the explanation of the fact is difficult. It is possible that the giant cell represents a capillary that has become thrombosed, if we accept this view as to the origin of giant cells; but more than this cannot be said.

Tuberculosis is often found at an autopsy in the miliary form. The organs are then sometimes seen to be more or less thickly covered by a number of greyish semi-translucent grains, and some of them are to be found in the substance of the organs. It can hardly be said, however, that the general form in which the miliary tubercle is found is a greyish-translucent grain, for the process of caseation sets in so rapidly that one usually finds a number of minute yellowish-white grains.

If one examines sections of a single discrete tubercle of somewhat larger size, one finds that the centre is occupied by a mass of caseous material, and that immediately around this there is a small number of giant cells which are, in their turn, surrounded by layers of epithelioid cells and lymphoid cells. However large the single tubercle may be, it is composed of no more than these layers, and we are forced to conclude that it grows peripherally while it caseates centrally. In course of its extension it impinges upon the margins of other tubercles, and by the coalescence of the originally discrete tubercles an irregular mass of caseous tubercle is produced. In all cases, however, so long as the mass of tubercle is extending, the layers of giant cells, epithelioid cells, and lymphoid cells are found at the periphery in the same order of arrangement as in the miliary tubercle.

Where the mass of tubercle during its extension comes into contact with a tube which has connection with the outer air, even remotely, the softened caseous material in the centre of the mass of tubercle becomes discharged, with the result that a cavity is formed the walls of which consist of tuberculous granulation tissue. This condition obtains in the case of tuberculosis of the lungs, where the caseous material discharges into a bronchus and gives rise to the formation of a **vomica,** and in the case of the kidney, where the caseous foci discharge into the pelvis of the organ, giving rise to the formation of tuberculous abscesses. It is not even necessary that the softened caseous material should come into contact with a duct or other tube; it may point just like any other abscess. This is seen in the case of a psoas abscess, which is nothing more than an abscess connected with bone caused by a special variety of micro-organism, the B. tuberculosis. The same is true in the case of all other forms of tuberculous disease of bones and joints.

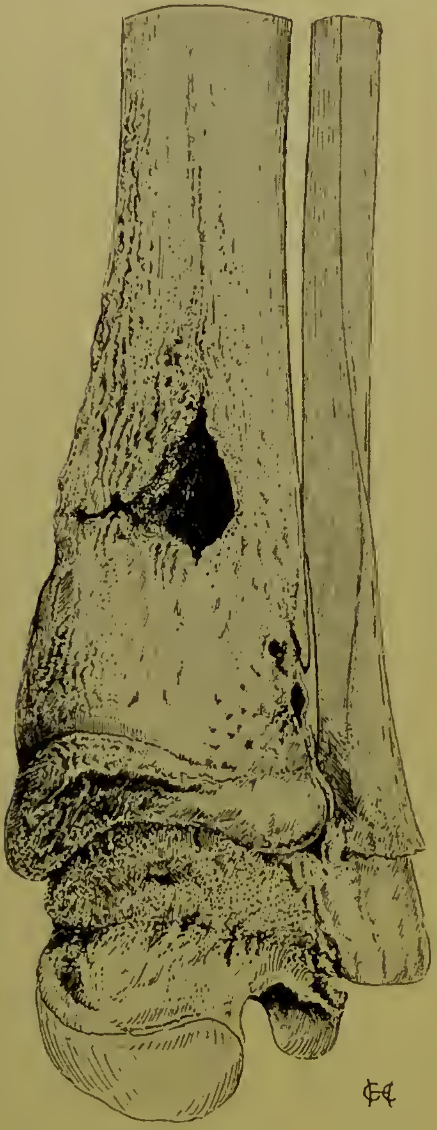


Fig. 21.—Tuberculous Caries of the Lower End of the Tibia. × $\frac{3}{4}$.

The bone is rough and very porous. At the principal seat of irritation a definite opening (bone abscess) has occurred. The tibio-astragaloid joint has become obliterated, after destruction of the cartilages, by formation of new bone.

So far as the actual lesion is concerned, therefore, the only difference between the inflammation in tuberculosis and any other inflammation lies in the chronicity of the process and the great tendency to the occurrence of caseation. So, too, in tuberculous, as in any other inflammation, there is a loss of tissue, and if the tuberculous irritant becomes arrested, repair is necessary. In this instance, as in others, repair is carried out by the formation of new fibrous tissue. Fundamentally, therefore, there is nothing to differentiate the tuberculous from any other chronic inflammation, with the exception of the cause. But if we can find the B. tuberculosis in the chronic inflammatory lesion our diagnosis can be an absolute one.

Unfortunately, it is often impossible to find the bacillus, and then we have to rely on other criteria. Thus, the situation in which the lesion is found affords very valuable information. If it be a lung, or an adrenal body, or a lymphatic gland that is affected with the caseous chronic inflammatory change, there is the strongest probability that we shall be right if we pronounce it to be tuberculosis. The same is true where joints and their synovial membranes are affected. But in the case of bone and of skin the matter is not quite so simple, for syphilis, which is equally a chronic inflammatory process accompanied by a great tendency to caseation, also affects these parts very frequently. But even then there are other differences which help one towards a decision. Into a consideration of these differences we cannot enter here; they will be more fully and more appropriately discussed in works on medicine and surgery. Here, we can only insist upon the fact that, although the cause of tuberculosis differs from the causes of other forms of inflammation, the lesion itself, being called forth as the result of the action of an irritant, does not differ *fundamentally* from the lesion called forth by any other irritant. The only true specificity of tuberculosis lies in its cause.

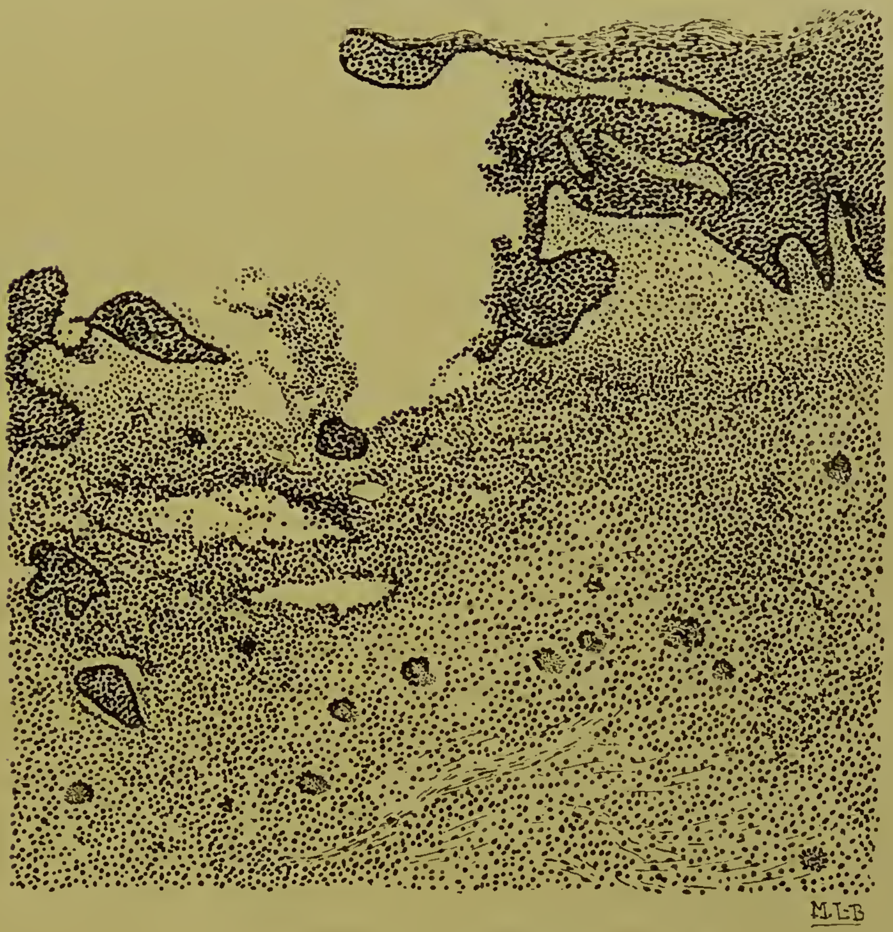


FIG. 22.—SECTION OF A LUPOID ULCER. × 60.

Above are seen the edges of the ulcerated epidermis to right and to left, in the centre being the ragged surface of the ulcer itself. Below is a granulation tissue without blood-vessels, but showing numbers of leucocytes, many giant cells, and a small quantity of young fibrous tissue. Cf. fig. 96.

To the subject of Lupus no separate attention will be given here; it is now generally allowed that it is merely a cutaneous manifestation of tuberculosis.

SYPHILIS

All the manifestations of syphilis are examples of granulation tissue, but in some the evidence of this statement is more striking than in others. Caseation is also very common under certain circumstances.

It is usual to divide syphilis into three stages, and in accordance with this clinical division a certain difference obtains between the portions of the body which are liable to be affected. The primary lesion (hard or Hunterian chancre) is usually situated upon the external genitalia, but its prevalence in this sitaution is due to the method in which the disease is contracted and not to any peculiarity of the tissues in these parts. For the primary lesion will manifest itself at any point, in an individual not previously the subject of the disease, at which the specific syphilitic virus gains access to the tissues. Thus a chancre will develop upon the nipple of a wet nurse if she is not syphilitic, and the child which she has to suckle is the subject of congenital syphilis. So, too, a chancre may form in the mouth as the result of smoking the pipe of a man who has manifestations of syphilis that are still infective in his mouth. And chancres are found, from time to time, in other abnormal situations.

The *primary* lesion of syphilis becomes fully developed about four weeks after exposure to infection. On the second or third day after infection, it is true that a small red spot may be seen which itches, but in a very large number of cases there is nothing to draw attention to the spot until a small slightly raised papule appears, which speedily ulcerates on the surface, and which gives rise to no pain or other inconvenience. This ulcer is situated upon a base of almost cartilaginous hardness, a point which, taken with other factors, affords important indications as to the nature of the inflammatory process.

A microscopical section of a hard chancre shows that it consists entirely of granulation tissue, with the newly formed capillary blood-vessels arranged in a series of lines running parallel to one another in a direction at right angles to the ulcerated surface and forming loops immediately beneath the free surface. Between the capillaries is a certain amount of young fibrous tissue with many fibroblasts, but more numerous are the small round cells which not only lie between the capillary loops but also infiltrate a considerable amount of the surrounding and underlying tissue. It is principally the number of these cells that occasions the peculiar hardness of the base of a hard chancre. Upon the surface is a thin layer of pus cells.

A very important and characteristic effect of the syphilitic virus is also commonly seen in such a section. It is one of the characteristics of syphilis that it has a special tendency to affect the endothelial lining of the small blood-vessels, particularly the arterioles, and induce a great proliferation of the cells constituting the intima (cf. fig. 72). This condition, which is known as **endarteritis obliterans**, in course of time produces so considerable a narrowing of the vessel, and so greatly interferes with the blood supply, that the tissues which derive their nutriment from the diseased vessels undergo degenerative changes of which the most common is caseation. It is not, indeed, customary to meet with actual caseation in a hard chancre, but the alteration of the vessel-wall is often to be seen in a very marked degree. Although there is the difference between the granulation tissue in tuberculosis and in syphilis that in tuberculosis blood-vessels are wanting, while in syphilitic granulation tissue they are present, the subsequent fate of the blood-vessels in syphilis practically reduces the two conditions to a common level, so far as the tendency to the occurrence of caseation in both of them is concerned.

The manifestations of what is called *secondary* syphilis are also inflammatory, but whereas late secondary manifestations are almost always built up on the type of granulation tissue, this is not so obvious in the case of the early secondary changes. About six weeks after the primary lesion has become evident, there usually appears a cutaneous rash which has certain characteristics as far as its distribution and appearance are concerned. Into these points we cannot here enter. Microscopical examination of one of the spots affords no special information as to the nature of the condition; evidence is only given of a mild dermatitis. That is to say, there is a slight local congestion of the cutaneous blood-vessels, a slight infiltration of the corium with leucocytes, and a slight tendency to desquamation of the most superficial layers of the epidermis.

At about this time localised foci of inflammation appear in the mouth, affecting probably the mucous membrane of the insides of the cheeks, in the folds between the nates, and sometimes in other places which possess in common with those that have been mentioned the characteristic of being moist. In these situations the local dermatitis is essentially of the same kind as that which affects drier portions of the skin, but a special character is imposed upon them by the fact that the moistness and relative looseness of the tissue in which the inflammation is taking place allow of a greater accumulation of cells and exuded fluid at the spot. As a consequence the focus of inflammation tends to be raised above the general level of the surrounding tissue. At the same time the effect of the irritation upon the epithelial cells and upon the underlying corium is shown by an increased growth of each. The inter-papillary masses of epithelum consist of more layers than usual, and the papillæ become elongated. There is thus formed an inflammatory growth which has some of the features of a papilloma, though the exuberant growth of the papillæ and their covering epithelium never gives rise to a dendritic appearance. In the mouth such inflammatory manifestations of syphilis are termed **mucous tubercles**; in the neighbourhood of the anus they are termed **condylomata.**

At a still later period of the disease, but still forming part of the so-called secondary manifestations, inflammatory changes occur about the soft palate and the larynx. These lesions offer certain points of marked contrast to those which precede them in time. They are apt to be far more extensive, to be associated with considerable destruction of tissue, and to be associated with very definite evidences of caseation. In these respects they have much in common with the tertiary manifestations of syphilis, and for this reason are by many authors regarded as being in this and not in the secondary group. From a pathological point of view, the distinction is an unimportant one, for no fundamental difference obtains between the histological appearances of syphilitic manifestations in any stage of the disease. But from a clinical point of view the matter is of fundamental importance, for it is generally accepted that an individual is capable of communicating the disease while he is the subject of primary or of secondary manifestations, but ceases to be specifically infective when he only suffers from tertiary symptoms. For reasons judged by this criterion, most authors class the pharyngeal and laryngeal troubles met with in syphilis as late secondary.

Tertiary syphilis manifests itself by the formation of masses of caseous inflammatory material which are known as **gummata**. Gummata may be formed in any situation, so that any special tendency which may be recognised in primary and secondary syphilis for the disease to affect certain parts, and to affect them in a more or less symmetrical way, is no longer evident. Nevertheless the prevalence of caseation amongst the tertiary lesions of syphilis stamps them with a peculiar character of their own. It has already been said that this tendency to caseation depends upon the liability of the arterioles to be seats of endarteritis obliterans. When a gumma has been formed, its subsequent history may be either that it softens in the centre and ultimately forms an ulcer (this is particularly the case with gummata in the skin and subcutaneous tissue), or the caseous material may be absorbed, and the former site of the gumma may ultimately be represented by a widely radiating and depressed cicatrix (as in the case of a healed gumma of the liver).

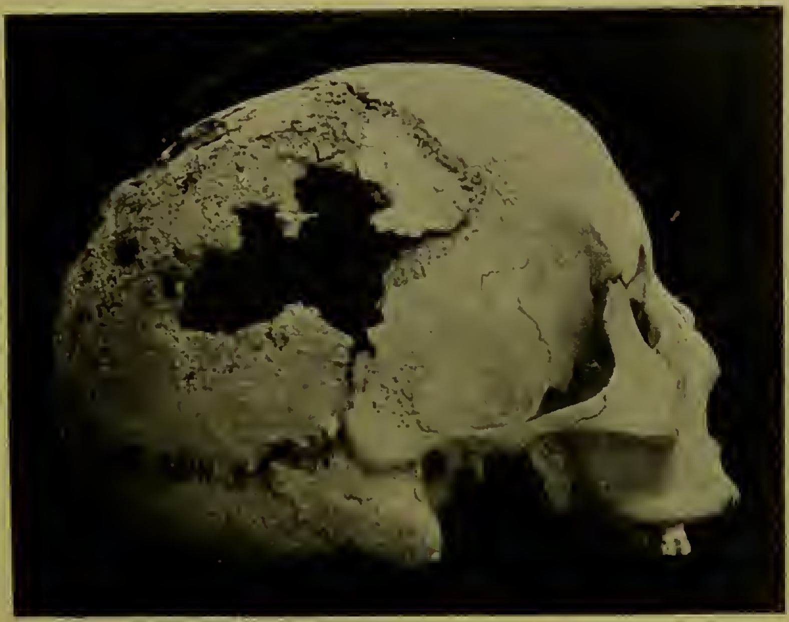


FIG. 23.—SYPHILITIC CARIES OF SKULL. × $\frac{1}{3}$.

A large portion of the bone has completely disappeared, and much of the remaining portion of the vault is worm-eaten and carious. (From a photograph.)

A series of phenomena has been described to which the term 'post-tertiary' has been given. They consist in certain diseases of the nervous system, and we shall consider them more fully later. It may here be stated, however, that there is weighty evidence for considering that the syphilitic poison is directly accountable for the occurrence of many of the scleroses of the central nervous system. The same is probably true also in the case of certain other fibroses, notably fibrosis of the myocardium, and at least one form of fibrosis of the liver.

Congenital syphilis.—There is no doubt that the offspring of persons who are the subjects of syphilis often offer manifestations of the disease. When one parent is the subject of primary or secondary (but not tertiary) syphilis, the fœtus often dies before term, and the occurrence of frequently repeated miscarriages is one of the commonest results of marrying too soon after contracting the disease. And even when a living child is born it will manifest, sooner or later, symptoms of the disease. Thus it may be born with cutaneous (secondary) lesions, or it may develop during the first weeks of life mucous tubercles about the angles of the mouth, or it may suffer from chronic inflammation of the nasal mucous membrane (snuffles). These are all secondary manifestations, and it is because of their presence that an infant, the subject of congenital syphilis, is capable of infecting other persons.

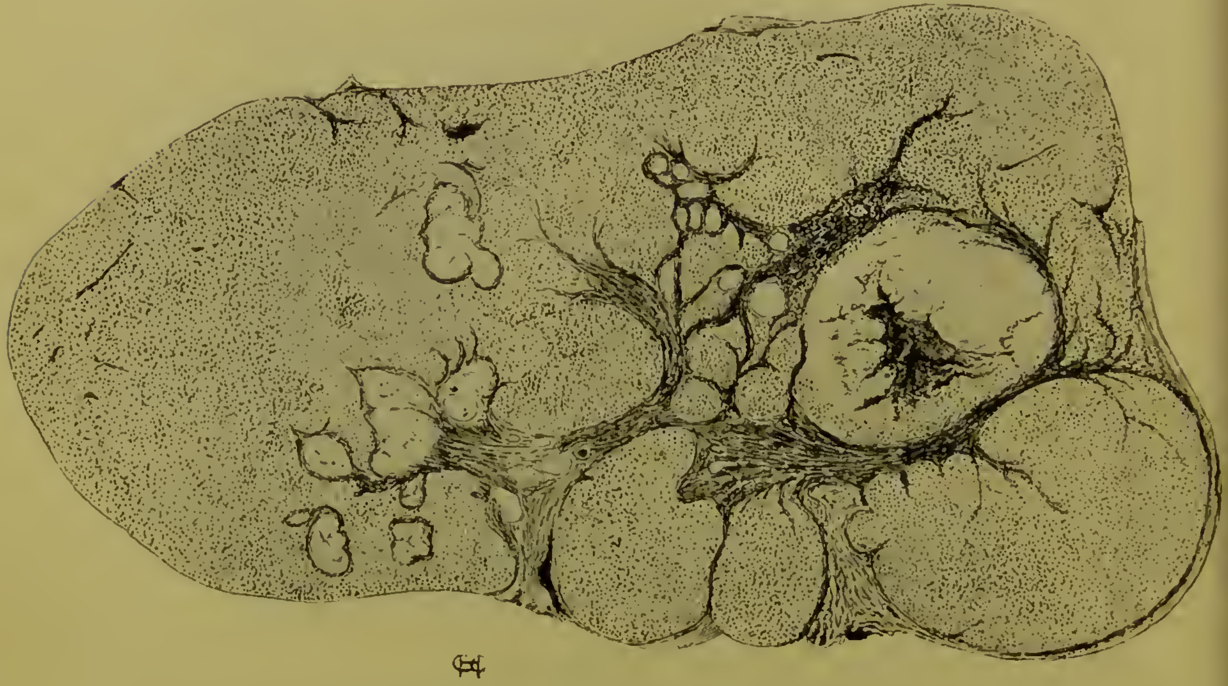


Fig. 24.—Gummata of Liver. × $\frac{2}{3}$.

Masses of caseous material are seen in the substance of the organ surrounded by much dense fibrous tissue.

Another manifestation of congenital syphilis is seen in the liver, an organ which, in acquired syphilis, remains free during the secondary stage of the disease but is frequently affected in the tertiary stage. Both in the case of premature stillborn infants, the subjects of congenital syphilis, and in those which are born at viable ages, it is not uncommon to find that the liver is the seat of an enormous overgrowth of fibrous tissue. It is true that one may find gummata of the ordinary kind in the livers of congenitally syphilitic children, but a far more common condition to find is an extreme inter-cellular fibrosis which is totally unlike any other fibrotic condition met with in the liver. Children having syphilis in this form rarely live for more than two or three years, and generally die during the first months after birth.

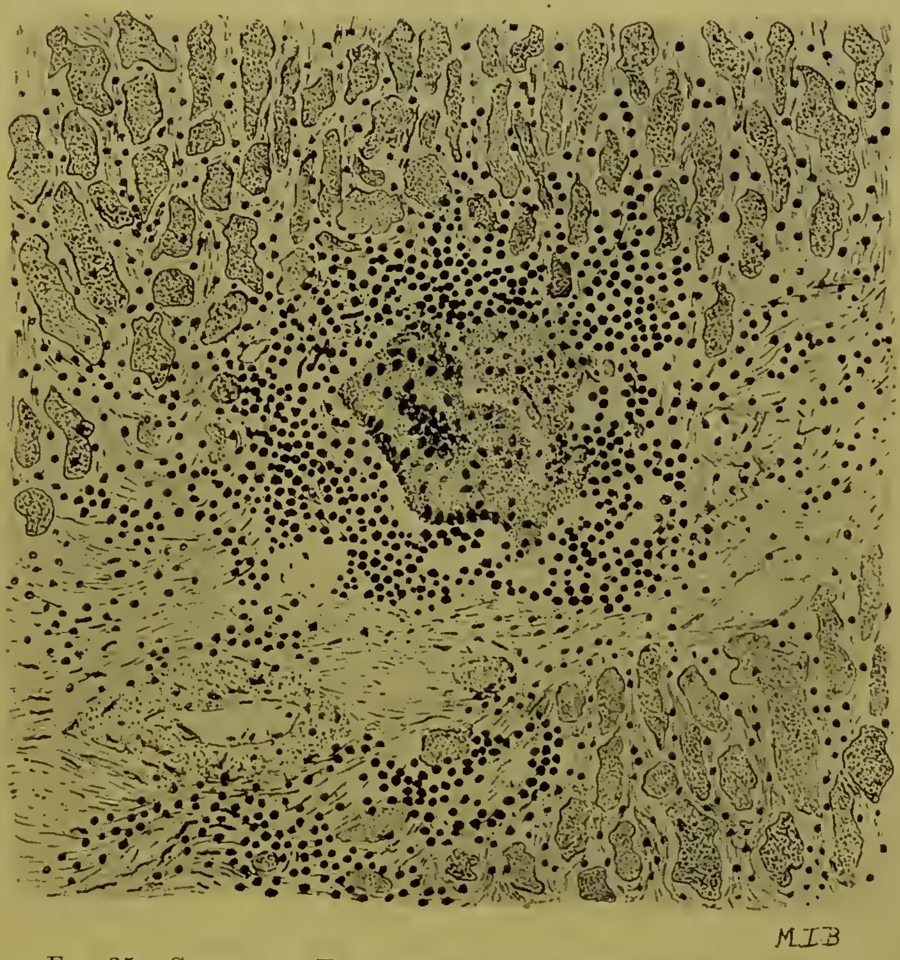


Fig. 25.—Section of Early Syphiloma of Myocardium. × 420.

The mass consists of a giant cell surrounded by leucocytes. Below and to the left of the nodule is a blood-vessel showing syphilitic alteration of the internal coat. There is a great excess of fibrous tissue and of leucocytes throughout the section, and the myocardial muscle has lost its striation and become granular. Cf. with fig. 20.

Later manifestations of congenital syphilis are seen in the permanent teeth, the two central upper incisors often being notched and peg-like in shape, and in a peculiarly intense form of multilobular fibrosis of the liver. These manifestations must certainly be classed as post-tertiary, and it may be noted in this connection that a few undoubted cases of disease of the central nervous system have been recorded, in all respects similar to those which have been classed as post-tertiary in the subjects of acquired syphilis.

Before leaving the subject of syphilis, it must be noted that, although it is commonest for tertiary manifestations to show themselves in the formation of gummata, this is not always the case. In the heart, for example, syphilis often shows itself by the formation of a very definite cellular infiltration of the inter-muscular connective tissue, with disappearance of portions of the muscular fibres. The cells in the inter-muscular septa are, in the main, small round cells, but there is also an increase in the number of young connective-tissue cells, and giant cells are also sometimes to be found. In such cases there may be a complete absence of endarteritis obliterans and of caseation.

ACTINOMYCOSIS

The disease caused by the **ray-fungus** or **actinomyces** is more commonly seen among cattle than among human beings, but it occurs in man with sufficient frequency to warrant a short notice here. Like the other diseases that have been just described, the lesion produced by the action of the irritant is built up on the type of granulation tissue, but it differs from the lesions of tuberculosis and syphilis in certain respects. Thus the actinomycotic nodule is more commonly made up of small round cells, and giant cells and fibroblasts are less frequently met with. Nevertheless both of these varieties of cell are, at times, to be found, and sometimes the giant cells are of exceptional size and contain an abnormally large number of nuclei. Upon the whole, however, it is commonest to find that an actinomycotic nodule consists of a number of small round cells resembling pus cells, and the similarity is the more striking in that the centre of the nodule is likely to break down into pus. There is, on the contrary, not the same tendency to the occurrence of caseation that there is in the cases of syphilis and tuberculosis. Indeed, the first information that the disease from which the patient is suffering is actinomycotic, is often given by the fact that the pus contains small spherical grains about the size of a pin's head. These on microscopical examination are found to be minute masses of the fungus.

The principal situations in which actinomycosis is found are the lung and the intestinal tract, particularly the region of the vermiform appendix. This is the case in man; in cattle it is commonest for the disease to be manifested in the tissues about the mouth, whether the tongue or the jaw. In the lower animals, too, there does not appear to be the same tendency for the masses of actinomycotic inflammatory tissue to break down into pus, but this may only be an example of the fact that suppuration generally is a far less common occurrence in the lower animals than in man. It will easily be concluded, from what has been said above, that though the diagnosis of actinomycosis is very easy when portions of the fungus itself are present for microscopical

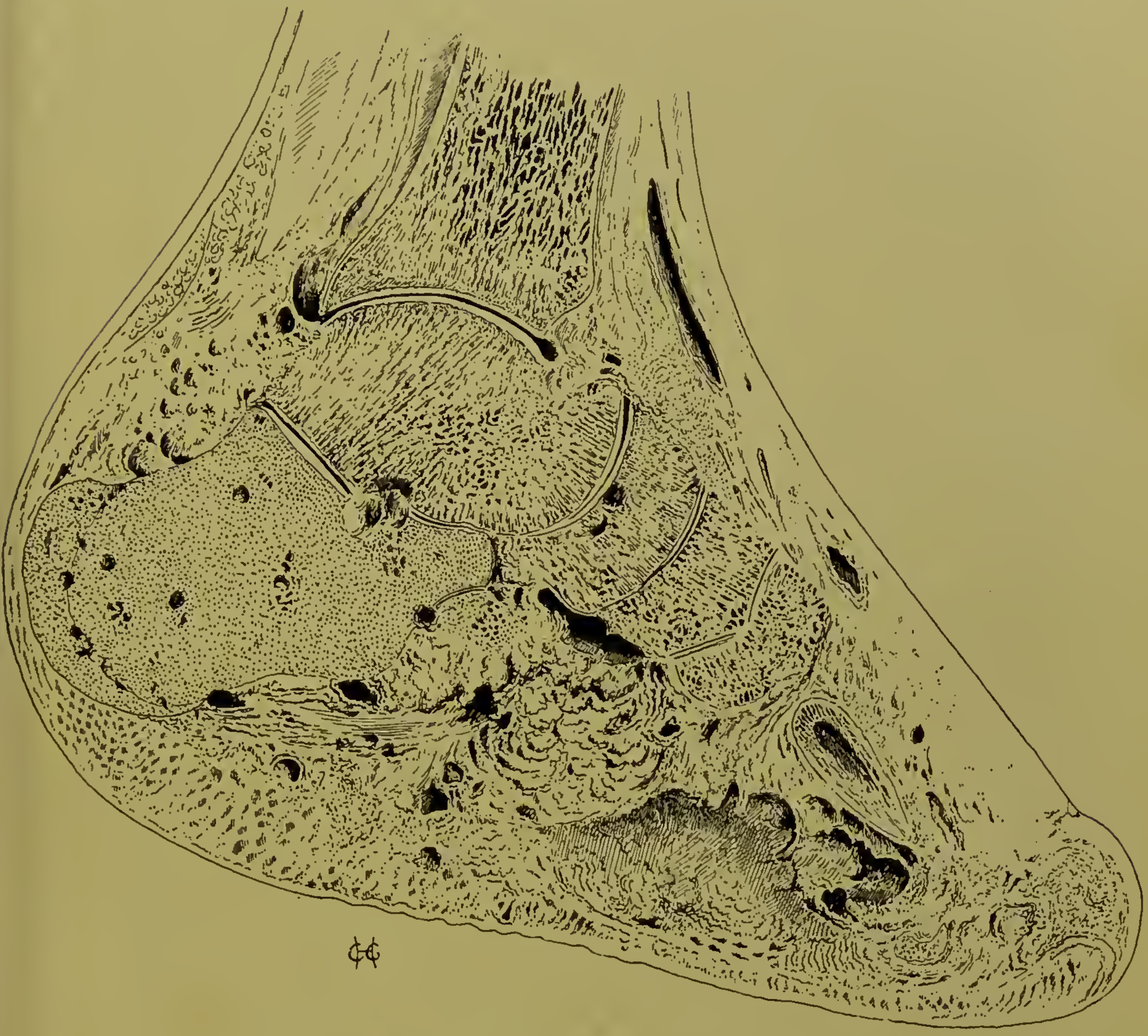


FIG. 26.—SECTION OF MADURA FOOT. × $\frac{2}{3}$.

The subcutaneous tissue and bone are infiltrated with inflammatory material, which has broken down at places into small abscess cavities that open on the surface by sinuses. The bone itself is porous and carious. Masses of the streptothrix are found throughout the part, and give it a blackish appearance. Similar changes are found in actinomycosis of the jaw, but without the black appearance, which is due to the spores of the madura fungus.

examination, it is practically impossible to diagnose the disease in their absence.

From a bacteriological point of view, actinomyces is classed among the Streptothrices, a group of organisms concerning which we know very little beyond the fact that they bear close similarities to one another, and are causes of more morbid conditions in man than was imagined a very short time ago. We must expect in the near future to learn that a number of conditions, the causes of which are at present unknown, depend upon the action of some one or other of this class of organism.

GLANDERS

While it is probable that actinomycosis is contracted by man in much the same way as it is contracted by animals, viz. through the food, there is no doubt that the most important manner in which man contracts glanders is by direct infection from a horse, mule, or ass already suffering from the disease. This disease, which is caused by the B. mallei, appears in lower animals, in two forms, the one acute (glanders), the other chronic (farcy). In man, on the other hand, the chronic form is but rarely seen. In both instances the lesion caused by the specific bacillus consists of a low form of granulation tissue which very readily breaks down into pus and forms an ulcer. In the horse, the disease affects, almost exclusively, the nasal mucous membrane, but in man, though the nasal mucous membrane is at times found to be affected, it is commoner to meet with a cutaneous pustule or ulcer, and later in the disease with a general pyæmic condition.

So far as the occurrence of central softening of the mass of glandrous granulation tissue is concerned, the disease seems to stand about midway between syphilis and actinomycosis. That is to say at the autopsy of a person who has died from glanders we may find a suppurative condition beneath the pericranium, or even a suppurative meningitis, together with the presence in the lung of a number of caseous foci which can hardly be recognised by the naked eye from those which owe their origin to the B. tuberculosis. As might be anticipated, a most important point in attempting to arrive at a clinical diagnosis is the fact that glanders almost exclusively occurs in persons whose duties bring them into close contact with horses, &c. Ultimately, in the horse, also, the disease, if it be allowed to run an uninterrupted course, terminates by a general pyæmic infection.

LEPROSY

Leprosy differs from all the diseases we have discussed hitherto in the fact that though the existence of a special micro-organism has been determined *in* the particular lesion which constitutes the disease, we cannot as yet say that this organism is the cause of the disease. For attempts to cultivate the bacillus in question have hitherto failed. The disease is practically never met with in the United Kingdom at the present day, except in the case of persons who have contracted it elsewhere. But it was formerly endemic. Nor is it generally met with in Europe, though it is found with fair frequency in Norway and Iceland. In tropical regions, and particularly in the neighbourhood of the coast, it is of very frequent occurrence.

The disease has many points of similarity with tuberculosis, indeed pulmonary tuberculosis is one of the commonest of causes for the ultimate death of leprous patients. It affects principally the skin, forming in it a number of subcutaneous nodules which microscopically consist of granulation tissue in which all other elements are subordinated in point of numbers to the cells of epithelioid character. It does not, however, affect the skin alone, nodules of leprous inflammatory tissue being found in nerves, in the larynx, spleen, and in other situations. While it is true that when they affect the skin the leprous nodules consist principally of cells of the epithelioid type, this is not so when the nodules are found in other situations. They then usually offer a greater variety of structure. Nodules occurring in the larynx, for example, may show a considerable number of giant cells, and whenever the nodules have a great tendency to break down, the number of small round cells entering into their composition is usually large.

This is not the place to enter into a description of the clinical characters of leprosy, but it may be stated that four chief varieties are recognised. These are: (1) lepra tuberculosa, in which there is a formation of subcutaneous nodules; (2) lepra ulcerosa, in which the nodules show a marked tendency to break down and form ulcers; (3) lepra anæsthetica, in which the disease, by forming its inflammatory products in the course of, and in the sheaths of, the nerves, leads to hyperæsthesia followed by anæsthesia; and (4) lepra mutilans, a variety which is merely a subdivision of the anæsthetic form, and arises because the anæsthesia prevents a due recognition of the fact that the limb in question is exposed to injury. It is commonly held that the leprosy bacilli are contained in the cells of the leprous nodule, but evidence has been brought forward to show that, at all events in the case of the giant cells occurring in the leprous nodules of the larynx, the bacilli are situated in dilated lymphatics. This consideration has, of course, an incidental bearing upon the nature of the giant cells themselves.

SECTION V.

THE CHRONIC FIBROSES

During the discussion of inflammation and the processes that constitute repair, it has often been said that the ultimate end of all the phenomena concerned is the formation of a new fibrous tissue. Under certain circumstances this fibrous tissue becomes exceedingly dense, and its histological characters are somewhat definite, so that we speak of it as scar tissue.

In the cases which we have hitherto considered it has been certain that the formation of this dense fibrous tissue was preceded by a condition of inflammation, but in some situations we find a plentiful supply of adventitious connective tissue and yet cannot with certainty connect it with the previous existence of an inflammation. To newly formed fibrous tissue of this description we may nevertheless apply the term 'chronic fibrosis,' leaving it open as to whether it is a sequel to inflammation or not. As to the view that we are to take of the matter of its origin, a word will have to be said later.

Chronic fibrosis is not met with in all tissues, nor even in those tissues which it affects is it equally common in all. It occurs most frequently as a pathological condition in the kidneys, the liver, the central nervous system, and the heart. As a senile, and what may perhaps be almost considered as a physiological, condition, it is extremely common. It is then associated with atrophy, so that senile atrophy and senile fibrosis are terms which almost denote the same macroscopic condition. The ovaries and testes in old age rarely fail to give evidence of the change, but it is far commoner in the ovary than in the testis. Nevertheless, fibrosis of the testes does occur as a distinctly pathological condition; it is a frequent result of syphilis.

In yet a third set of cases it is difficult to decide whether the fibrosis which obtains should be classed as pathological or physiological. It is met with in tissues which have never taken on the function to which they were destined. Thus an undescended testicle, which is always functionless, is also the seat of a well-marked fibrosis. A somewhat similar, but much more erratic, formation of fibrous tissue is seen in the case of the fibro-myomata : these growths occur in the uteri of sterile women with more frequency than in the uteri of multiparæ. Reference will be made to them in the section upon the Tumours.

To the senile fibroses it is not necessary to refer in detail. For they differ only in extent from the definitely pathological fibroses, being, as a rule, much less well marked. The same is true of the fibroses of the third class.

The essential condition in the existence of a chronic fibrosis is, of course, the presence of an excessive amount of a fibrous tissue which is not normally present in the affected organ. This fibrous tissue does not restrict its presence to situations in which it is normal for fibrous tissue to be found, but it invades the essential elements of the organ and divides it up into a number of irregular masses which may be small or large according to circumstances. This is particularly the case when the liver is the organ affected, and then it is usually easy to see with the naked eye the presence of a number of fibrous-tissue bands of varying width, traversing the organ in all directions. The same is true in the case of the kidney when it is the seat of chronic fibrosis, but not to the same extent. For in the kidney there is a tendency for the newly formed connective tissue to run on lines that have previously been laid down, so that we meet, in this organ, with an excessive development of the pre-existing stroma. Nevertheless in the kidney, too, there is a new formation of connective tissue which invades the essential renal substance.

The liver and the kidney are more closely allied, so far as the appearances produced by the occurrence of chronic fibrosis in them are concerned, than the other organs which have been mentioned as seats of the change. In the heart, chronic fibrosis is a far less common phenomenon than it is in the liver or the kidney, and at the same time it is far less regular in its arrangement. There is no semblance of a restriction to the normal connective-tissue framework of the organ, but the masses of fibrous tissue are distributed in a haphazard way throughout the organ. In the central nervous system, when fibrosis occurs, it always involves a definite section or tract, at least secondarily. Primarily, we have reason to believe that it may occur in the same irregular manner as in the heart (cf. figs. 69, 103, 131, 140, 165).

The variety of fibrous tissue which is found in these different cases is always the same. It is always extremely dense and avascular, and contains few connective-tissue corpuscles, and those which are present are contracted and angular. The bundles of fibres are not arranged in an orderly manner, but on the contrary, they interlace in all directions. With the exception of the central nervous system the irregularity of the arrangement is such that portions of the organ which they affect are cut off from the rest, and lie in the midst of a mass of fibrous tissue. It is in this manner that their atrophy is brought about, for in the immediate neighbourhood of the mass of fibrous tissue, the included portions of the tissue of the organ are always less numerous and of smaller size than they are at some little distance away.

So far as the actual nature of the process at work is concerned it was not unnatural, seeing the resemblance of the fibrous tissue present in the cases now under consideration, for the earlier workers to conclude that they had to deal with an extremely chronic variety of inflammation—an inflammation so chronic, that is, that they never saw the commencement but only the end. For this reason the termination denoting inflammation (-itis) was used in the nomenclature, with the result that the conditions were spoken of as 'chronic nephritis,' 'chronic hepatitis.' In the case of the fibrotic condition of the heart the name 'chronic myocarditis' was also used at times, but far more commonly the condition was spoken of as 'fibroid degeneration.' In the case of the central nervous system, the termination '-itis' was never used, but the condition was known as 'sclerosis.' In the case of the nervous system, too, it was never held that the condition is inflammatory, but it was fully recognised that the new formation of fibrous tissue comes about to fill the place of nervous elements that have degenerated.

But in spite of the fact that in recent years there has manifested itself a growing tendency to regard the fibrotic conditions as being independent of inflammation, there still exist many notable pathologists who cling to the inflammatory view, at least in the case of the liver and the kidney. It is therefore impossible to speak dogmatically upon the point.

The whole question practically turns upon the point as to whether the formation of the new fibrous tissue precedes the destruction of the essential elements of the organ in which the fibrosis is taking place, or whether the essential elements degenerate first and the formation of connective tissue succeeds, in the same way as it is admitted that it does in the scleroses of the central nervous system. Numerous experiments have been made with the object of deciding the point, but as yet they have not proved the matter conclusively one way or the other.

It is certain, however, that we occasionally meet with a condition of true interstitial inflammation of the liver, in the sense that the changes are most marked in the connective-tissue framework, and that they consist in the presence of a great number of leucocytes such as we know are characteristic of inflammation in other parts. Here the inflammation is acute, and it may concern a liver which is, or is not, the seat of a chronic fibrosis. From this it would seem that the two conditions are distinct. The more so, since it would certainly be a matter for remark that organs which are so intensely vascular as the liver and kidney should manifest the signs of acute inflammation less commonly than they do signs of chronic inflammation (chronic fibrosis).

SECTION VI

THROMBOSIS, EMBOLISM, AND INFARCTION

In this section we shall have to consider the effects of certain morbid conditions of the blood-vessels both as concerns themselves and as concerns the tissues with the nutrition of which they are connected.

THROMBOSIS

Thrombosis consists in the formation of a coagulum within the vessel. The condition affects both arteries and veins ; but, for reasons that will appear later, thrombosis of veins is far more commonly seen than thrombosis of arteries. In the case of capillaries, thrombosis is of particularly common occurrence, as it is rarely absent from any focus of inflammation. It is also of frequent occurrence in the cavities of the heart.

The mass of coagulum which constitutes an essential part in the process of thrombosis is often termed a **thrombus**. Thrombi are of two distinct kinds, red and white, and the mode of formation of the two varieties is different. A *red* thrombus owes its colour to the fact that the clot has been formed from blood under such conditions that the red blood corpuscles are entangled in the meshwork of fibrin. A *white* thrombus, on the other hand, is one in which few, if any, red blood corpuscles are to be found. Between these two extremes we have a number of gradations in colour, and therefore in the extent to which red corpuscles enter into formation of the clot. In addition to the varieties of thrombus already mentioned, mixed thrombi are very frequently met with : in them one portion of the coagulum is white, while the remainder is red.

For the formation of a red thrombus it is necessary that the process of coagulation shall take place with a fair degree of rapidity, so that the red corpuscles shall not have time to subside owing to their superior specific gravity. A white thrombus, on the contrary, is formed with far less rapidity, unless it be formed in such a situation as a lymphatic, where the number of red cells is usually very small. We may leave thrombi in lymphatics out of the question, however, because of their comparative rarity. It is further a characteristic of white thrombi that the fibrin of which they are composed is deposited locally from the still circulating blood. Mixed thrombi are formed from blood which is at rest, as, for example, in the cavities of the heart after death. In them, coagulation does not occur until the red cells have had time to become deposited, and hence the uppermost portion of the thrombus is colourless, and is separated by a distinct line from the continuous deep portion of the same clot, which is dark red, purple, or even almost black.

Associated with the different methods of their formation white and red thrombi bear different relations with the vessel-wall. A red thrombus is never adherent to the vessel-wall, but can be drawn out from the vessel much in the same way that a blood clot can be drawn out from a test-tube into which the blood has been placed before clotting. A white thrombus, if we except those conditions in which the coagulation takes place in a blood stream that is moving very sluggishly, as for example during the last hours of life (agonal thrombus), and the rare instances of coagulation in lymphatics, is always adherent. This difference enables us to determine whether a given thrombus has been formed during the life of the patient or only after death a matter often of great importance.

It is unnecessary to enter in detail into the histological appearances of the various kinds of thrombus, for they obviously only consist of fibrin with or without an admixture of red cells. It must be noted, however, that since a white thrombus is formed from the circulating blood, the fibrin of which it consists is deposited in successive layers which are commonly recognisable with ease. When the formation of a white thrombus has proceeded to such a degree that it encroaches to a considerable extent upon the lumen of the vessel, the obstruction is completed by the formation of red thrombus. It need hardly be stated that the flakes of fibrin which separate out of an exudation, whether inflammatory or not, into one of the serous cavities, are, in reality, identical in constitution, though not in arrangement, with a white thrombus.

Concerning the method in which a red thrombus is formed there is little doubt. Apparently the separation of fibrin from the stagnant blood first of all takes place at various points on the wall of the containing vessel, and thence proceeds towards the centre of the mass of blood. In the case of white thrombi there is more uncertainty. It is certain that for the formation of a white thrombus it is necessary that there should be some lesion of the endothelial lining of the vessel, but the very first stages of the processes which culminate in the formation of the white thrombus are more doubtful. By some authors it is held that the first step consists in the accumulation at the spot of a number of blood platelets, and that it is by the action of these upon the fibrinogen of the blood that the first beginnings of the thrombus are produced. By other authors it is held that the first step consists in the accumulation of a number of leucocytes at the point of lesion, and that these form fibrin ferment, which combines with the fibrinogen of the layer of blood in immediate contact with them. Certainly we find a considerable number of instances in which the accumulation of leucocytes in the neighbourhood of the lesion is a very early and the sole recognisable change, so that for the present we may conclude that, though the accumulation of leucocytes may, perhaps, not be the very first step in the formation of a white thrombus, it is, nevertheless, an extremely early step (fig. 27). Once the beginnings of a thrombus are formed there is no difficulty in understanding the method whereby the coagulum increases in size. For the minute thrombus constitutes a foreign body in the vessel, and, as such, forms a point upon which fibrin is deposited, as it would be in the case of any other foreign body.

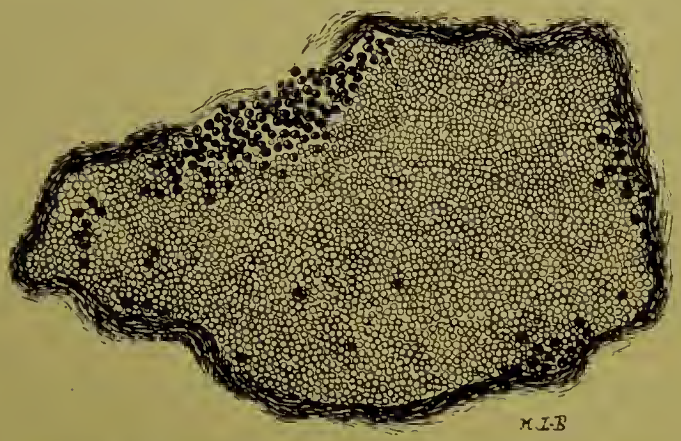


Fig. 27.—Section of Venule showing Commencing Thrombosis. × 300.

At the seat of injury has occurred a collection of leucocytes. Similar but smaller collections are found below and to the right, where the endothelial lining of the vessel had been damaged.

The conditions which lead to thrombosis are those intimately concerned with coagulation of blood generally. Of these alteration in the relation of the lining endothelium of the vessel-wall to the contained blood, and increase in the coagulability of the blood itself, are the most important. Frequently these two factors act together, as, for example, towards the latter end of an exhausting disease. Thus, in typhoid fever it is not uncommon for thrombosis to occur, and in this disease we have an alteration in the relation of the vessel-wall to the blood ; for, owing to the feebleness of the heart, the circulation is carried on less vigorously than normal, and the endothelium of the vessels suffers in its nutrition, and at the same time the fever, the diarrhœa, &c. lead to an increase in the coagulability of the blood itself.

But the cause of a thrombosis must not always be sought within the vessel-wall. Frequently the endothelium becomes involved by the extension of some morbid process beginning either in the vessel-wall itself or in the perivascular tissues. As an example of a thrombosis which depends upon changes occurring in the vessel-wall itself, we may cite the thrombosis which so commonly takes place when the walls of arteries are the seat of atheroma, with or without calcification, while the thrombosis which occurs in the neighbourhood of any focus of inflammation is perhaps, in the majority of cases, due to an extension of the inflammatory process from parts at a distance from the vessel-wall itself.

The effects of a thrombus upon the rest of the body depend upon a great many considerations, of which the chief are the situation, the size, and the question whether the thrombus is septic or aseptic. The last-mentioned point we shall consider when discussing the fate of a thrombus.

It is a matter of great importance for the tissues whose blood supply is implicated by the occurrence of the thrombosis whether the coagulation takes place in an artery or a vein. If it be a vein which is affected, the results may not be serious owing to the free anastomosis of these vessels. But this is only the case if the vein is relatively a small one, and if the thrombosis is not dependent upon a cause which equally affects the main vein and its anastomoses. We may therefore leave on one side the cases in which an aseptic thrombosis occurs in a limited part of the venous system; for, excepting that the affected vein is painful and hard to the touch, and that it may be the starting-point of an embolus, it gives rise to no changes in distal parts. But when a main vein, and practically all its anastomotic branches, are thrombosed, it is clear that no blood which is carried to the part by the still pervious arteries, can follow the usual course. A condition of the most extreme venous congestion is therefore set up, and the subsequent events are determined by that fact. If the obstruction to the venous return be not absolute, although very severe, there will be poured out a large quantity of passive exudation, and the part will become intensely œdematous. Such a condition is well seen in the case of thrombosis of the femoral and iliac veins after parturition (phlegmasia dolens), where the lower limb becomes white, the skin intensely stretched and glistening, and where the pain is acute from the large amount of œdematous fluid poured out into the subcutaneous tissue. If the venous obstruction is still more severe, moist gangrene occurs.

The importance of thrombosis occurring in arteries depends upon the fact that it implies either a very diseased condition of the arterial walls themselves, or great feebleness of the heart, or a combination of these two factors. In addition, the smaller united sectional area of the arterial system, and the fact that the arteries supply purified blood, combine to lend to arterial thrombosis a severity far beyond that which attaches to a venous thrombosis of equal extent. The chief morbid conditions under which thrombosis occurs in arteries are atheroma and syphilitic endarteritis; in both cases there is a diseased condition of the arterial wall, but in atheroma there is generally superadded a greatly enfeebled state of the heart.

The effects of an arterial thrombosis upon the tissues which the affected artery formerly supplied with blood, differ in different cases, but, apart from the question whether the thrombosis occurs as a part of a wider septic process, they principally depend upon the nature of the artery, so far as anastomosis is concerned. In this matter we are trenching upon the question of embolism, which is the chief cause of arterial thrombosis other than those which have already been mentioned. Thrombosis of arteries, along with embolism and its effects upon the tissues, will be considered when we are discussing embolism and infarction; here it need only be said that, when what we may call *primary* thrombosis occurs in the arteries, the condition of the anastomotic branches is generally so little better than that of the thrombosed vessel, that maintenance of a proper circulation is out of the question, and a more or less extensive local death of the tissues takes place. Perhaps the commonest cause for senile gangrene is a thrombosis occurring in highly atheromatous arteries of the lower limb, partly as the result of the alteration of the vessel-walls themselves, and partly as the result of the weakening of the force of the heart.

Fate of a thrombus.—In the case of the arteries especially, but also in the case of the veins, once a thrombus has formed, there is a tendency for it to increase in size by extending further along the vessels. Such increase in size, however, does not take place, as a rule, in the same way as obtains when the primary thrombus was being formed. Whether it is white, red, or mixed in character, the primary thrombus is adherent to the vessel-wall, but this is not the case with the secondary thrombus, which is non-adherent and red, being formed in the column of stagnant blood on either side of the primary thrombus. Secondary thrombus always extends as far as the next branch above and below the seat of primary thrombosis; whether it extends further depends upon the condition of the circulation and the nature of the cause which leads to the thrombosis.

Certain other changes may arise in the subsequent history of a thrombus besides its extension. If the thrombosis has resulted from the implication of the vessel in an inflammatory process which has started at some distance from the vessel, the subsequent history of the thrombus is practically determined by the nature of that inflammatory process. Where it is septic, there is a tendency for the thrombus to break down. This is especially the case where the thrombosis has occurred in connection with a neighbouring suppurative focus. Under these circumstances it is practically certain that the thrombus, or a part of it, will break down into pus, and both vessel-wall and clot will become merged in an abscess. As a rule, this suppuration of the thrombus does not involve the entire clot, but portions at either end remain unaffected, and, being reinforced by the formation of a certain amount of adherent clot, shut off the localised suppurating portion of the clot from the general circulation. If it were not for this fact, the suppurative process could not fail to be disseminated throughout the body. Such a condition sometimes occurs, and leads to pyæmia, but fortunately it is the exception and not the rule, for the reason that has been given.

In the case of the, frequently, large thrombi of the heart, a central softening is occasionally seen which leads to the formation of a fluid having all the macroscopic appearances of pus, but which is not pus. Reference to this change will be made later.

The last change that we shall consider here, which a thrombus may undergo as a part of its subsequent history, is **organisation.** When this takes place the lumen of the vessel is no longer filled with a mass of fibrin, but with a mass of true fibrous tissue which is firmly adherent to the vessel-wall, and which is formed by a process identical with that which leads to the replacement of the mass of fibrin that lies between the two lips of an incised wound. It is unnecessary to enter into the details of the method whereby the change is brought about; it need only be said that the red clot becomes decolourised, that into it penetrate new capillary blood-vessels derived from the vasa vasorum, and young connective-tissue cells derived from the pre-existing connective-tissue cells in the wall of the vessel, and perhaps also from proliferated endothelial cells. Not infrequently some of the newly formed blood-vessels within the former lumen of the vessel remain and become enlarged; in this way a channel or channels may be formed which connect the lumen of the vessel above and below the otherwise obliterated portion. Such a condition is termed 'canalisation' of the clot.

EMBOLISM

An embolus is a mass of material which becomes lodged at some point in the vascular system while circulating in the blood stream. Emboli of macroscopic size are found in arteries alone, and in them at some point at which the lumen of the vessel is diminished in diameter, e.g. immediately below a point at which it has given off a branch of considerable size, or where it bifurcates. Microscopic emboli, on the other hand, become lodged in the capillaries, whether systemic or of the portal or the pulmonary system: here they are to be recognised, not by their individual presence, but by the effects which they produce upon the surrounding tissues.

Emboli may consist of any kind of material, but the most common are portions of an already formed thrombus, small collections of micro-organisms, and portions of malignant new-growths. Under certain circumstances, bubbles of air or fat droplets may form emboli. Macroscopic emboli almost always consist of portions of pre-existing thrombi, and, as a moment's consideration will show, the commonest situations of thrombi which are followed by embolism are the left auricle and ventricle, including the aortic and mitral valves (in the case of embolism of one of the systemic arteries), the larger veins, and the right auricle and ventricle (in the case of embolism of the pulmonary artery and its branches).

Microscopic emboli produce changes in the tissues in the neighbourhood of the spot at which they are lodged by virtue of the substances of which the emboli consist. If they are derived from a septic source, and wholly or largely consist of pathogenetic organisms, they lead to a local manifestation of the disease with which they are primarily concerned. Thus they may be the cause of secondary abscesses, as in the case of pyæmia, or the cause of secondary nodules of tubercle in disseminated miliary tuberculosis. When the embolus consists of a small portion of a new-growth, the focus at which the embolus becomes lodged ultimately shows the presence of a secondary nodule of new-growth of the same kind as that from which the embolus was broken off. In either case the originally microscopic embolus may become the starting-point for the formation of a very considerable mass of diseased tissue. It is, of course, obvious that the question as to whether an embolus is aseptic or septic has the greatest influence upon the subsequent changes which are undergone by the tissues in the neighbourhood of the embolus, and that this question has nothing to do with the large or small size of the embolus itself.

Owing to the freedom of anastomosis which obtains among the capillaries, a capillary embolism is of no importance to the economy if it is aseptic or if it consists of material which is incapable of growth. This is not the case with emboli of larger size. With them a number of changes (infarction) are immediately produced which depend upon the size alone, quite apart from any other character of the embolus. No doubt other characters of the embolus—such, for example, as to whether it is septic or consists of a mass of a malignant new-growth—produce *subsequent* modification of the changes introduced by the size of the embolus, but with these we are not now concerned; so far as these factors modify the process, there is no difference between large and small emboli.

Sometimes the embolus is so large that it causes death of the patient within a few minutes. This is particularly the case when a portion of a thrombus, formed in one of the large veins such as the venous sinuses of the uterus after parturition, or the femoral vein, is suddenly dislodged, and, travelling by way of the inferior vena cava and the right side of the heart, becomes impacted in the pulmonary artery at its commencement or in one of its primary divisions. Smaller emboli produce less severe symptoms, and it is only to the action of very small emboli that we can ascribe the formation of hæmorrhagic infarcts (p. 135).

In addition to the changes which may be produced in the tissues normally supplied by the vessel which has become obstructed by the lodgment in it of an embolus, certain alterations occur in the vessel itself under any circumstances. The embolus constitutes a foreign body in the lumen of the artery, and besides obstructing the flow of blood through it, leads to the coagulation of the blood which lies between the embolus and the nearest branches, both above and below. The embolus thus comes to form the centre of a tapering thrombus which is usually shorter and wider on the proximal side of the embolus than it is on the distal. The subsequent fate of the embolus and its attendant thrombus is determined by such considerations as the septic or the aseptic nature of the embolus, &c., considerations which need not delay us now.

INFARCTION

When an embolus is lodged in an artery the effects which it produces upon the tissues which derive their blood from that artery vary within considerable limits and under different circumstances. If the artery is one having a number of freely anastomosing branches, the tissues themselves only suffer momentarily by the failure of blood to reach them by the usual channel; in a very short space of time the normal amount of blood reaches them, though by an indirect route, and the only effects of the embolism are purely local to the artery itself.

But where the artery is not provided with a number of anastomosing branches, and, in particular, when it is a 'terminal' or 'end' artery, the case is different. For here it is impossible for blood to be conveyed to the part served by the blocked artery, and the consequence is that the part dies. Owing to the fact also that such blood as was in the capillaries of the part before it became blocked by the embolus passes on into the veins, the dead tissue is of a white colour. The dead mass of tissue is shaped like a cone with the apex situated at the point of embolism; the base is generally situated on the surface of the organ in which the embolism has taken place. This shape is, of course, explained by the normal relation of the capillaries in connection with an end-artery and the main stem of the artery itself. This cone-, or on section, wedge-shaped mass of tissue is called an **infarct** or **infarction.**

An infarction, then, is a mass of dead material of a characteristic shape with its base on the surface of the organ, which owes its origin to the fact that the artery by which it is normally supplied with blood is of the terminal variety, and has become blocked by an embolus. Like any other mass of dead tissue it undergoes subsequent changes. At first the elements of which it is composed are clearly recognisable, but soon they become granular and fatty, and the distinctness of their outline becomes lost. Ultimately these degeneration products are absorbed, and a depressed cicatrix marks the former situation of the mass of tissue.

The method whereby the removal of the infarcted mass of tissue is carried out is practically identical with that which occurs in the healing of an aseptic wound. Very soon after the embolus has become lodged in the artery and the infarct has been formed, macroscopic examination shows that the white mass of dead tissue is bounded by a thin line of intense congestion. This congestion is, in reality, part of a mild inflammation resulting from the irritant action of the dead material upon the tissues surrounding it. By a series of changes which it is unnecessary to describe here, because they have been fully described when discussing the subjects of resolution and repair, the dead tissue is removed and its place taken by newly formed connective tissue. When the infarct is of very large size and is also aseptic, it may not be entirely removed. Under these circumstances the softened portion which is not removed remains encapsuled by fibrous tissue; it may even also become a seat for the deposition of calcium salts.

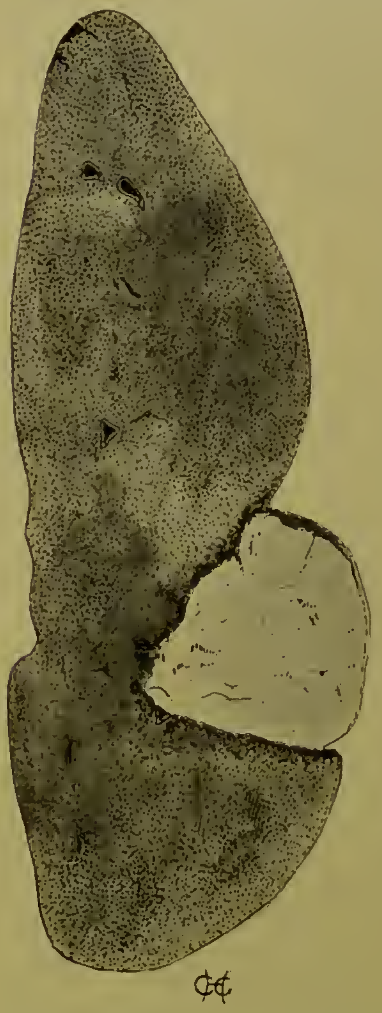


Fig. 28.—Anæmic Infarct of Spleen. × $\frac{3}{4}$.

A large colourless infarct of the organ is seen on the convexity. It is sharply defined from the rest of the splenic tissue.

Infarcts of the kind which has just been described are of common occurrence in the spleen and the kidney in cases of heart disease, especially those in which the mitral valve is concerned. But besides the anæmic variety of infarct, we meet with a variety which has been termed 'hæmorrhagic' from the fact that the infarcted tissue is crammed with red blood corpuscles. Practically the only situation in which the hæmorrhagic infarct is seen is the lung. The explanation of the process whereby this form of infarct is produced is somewhat difficult. It may be said, however, that the most commonly received explanations are that there is a hyper-engorgement of the veins and capillaries of the infarcted region due either (1) to the backward pressure of the blood in neighbouring capillaries and veins, or (2) to the persistence of a small pressure in the artery on the distal side of the obstruction. Be that as it may, there is no doubt that a microscopic section of a hæmorrhagic infarct of the lung shows the alveoli and such vessels as are visible to be crammed with red corpuscles in the midst of which strands of fibrin may be recognisable. Such an appearance is indistinguishable from one which is due to the direct rupture of a blood-vessel into a bronchiole, with the consequent filling of the infundibulum and air-sacs with blood (**pulmonary apoplexy**). Anæmic infarcts are sometimes found in the lung, and then the alveoli are filled with a serous exudation in which coagulation takes place, as is evidenced by the presence of a number of strands of fibrin. This occurrence of coagulation is more clearly seen in the case of anæmic infarct of the lung than in the case of anæmic infarcts of other organs. But no doubt can be held that the process is in all cases identical. The death of the tissues concerned in an infarction is brought about by a process of coagulation necrosis.

SECTION VII

THE NEW-GROWTHS OR NEOPLASMS

GENERAL

It is impossible to frame a definition of the new-growths which shall be entirely beyond criticism, but we may follow Ziegler and say that 'a tumour or neoplasm is a new formation of tissue which is atypical in structure, which subserves no useful purpose to the whole economy, and the growth of which has no typical termination.'

Such a definition serves to distinguish the neoplasm from a number of other formations which from their naked-eye appearance might claim to be included amongst the 'tumours' if irregular *swelling* were now, as was at one time the case, regarded as the chief criterion of the group. For the expression 'new formation of tissue' excludes from the neoplasms all cysts due to exudation or retention. The statement that a tumour is 'atypical' serves to eliminate all cases of generalised hypertrophy, that it 'subserves no useful purpose' eliminates such accumulations of newly formed material as provisional callus, while the statement that a tumour has 'no typical termination' separates the group from the whole class of inflammatory swellings and particularly from the group of so-called infective granulomata.

The new-growths have been classified in many ways. Virchow divided them into three classes, **histioid**, corresponding to some histological element in the adult body; **organoid**, corresponding to some one or other organ of the body; and **teratoid**, corresponding to no one definite tissue, but built up of the elements composing a complex system though imperfectly developed. The **teratoid** group is still recognised, and comprises all those tumours which are regarded as being dependent upon irregularities in the development of an impregnated ovum; they constitute the whole group of 'dermoid cysts.' The term **histioid** is still frequently employed to denote the simpler kinds of non-malignant tumour, but it is not used so strictly as was intended by Virchow; the term **organoid** has practically fallen into disuse.

Besides the terms given above it has been customary to speak of new-growths as **homologous** and **heterologous** according as they are or are not composed of tissue of the same nature as that in which they are situated, as **typical** or **atypical** according as they are or are not formed upon the pattern of some tissue present in the body in extra-uterine life, as **malignant** or **non-malignant**, and as **epiblastic**, **mesoblastic**, and **hypoblastic**, or more shortly, as being formed on the **epithelial** or the **connective-tissue** pattern. Certain of these terms need further explanation.

As examples of homology and heterology amongst tumours may be cited such tumours as are composed of bone. If the tumour is formed in connection with a bone, then it is said to be homologous, but if it is found in such a tissue as the lung, or the brain, or the testis, which do not normally contain bone, it is said to be heterologous. Concerning the use of the term *typical* in reference to tumours, little need be said. The tumour may consist of practically any of the elemental structures of the body, so long as it is a normal constituent of the body in extra-uterine life. Nevertheless the type is but rarely adhered to with strictness. To take one of the simplest examples: a fibroma is a tumour composed of fibrous tissue, and, as such, it consists of elements in every way similar to those of ordinary fibrous tissue. But it differs from ordinary fibrous tissue in its arrangement so definitely that it would be impossible for anyone on examining a microscopic section of a fibroma to imagine that the fibrous tissue was derived from a normal part. On the other hand, an *atypical* tumour is one which does not correspond with any tissue which is normally found in the body in extra-uterine life under normal conditions. But the tissue with which it does correspond is found in the body during intra-uterine life, and especially during the early days of development of the embryo. Here again we are confronted by a difficulty. It is true that all the tumours conserve the type of the animal, so that, for example, hairs and not feathers are found in tumours of man, and feathers, not hairs, in corresponding tumours of birds; but it is hardly correct to say that the epithelial and the connective-tissue cells of the embryo have no counterpart in extra-uterine life. For we cannot distinguish the rapidly growing epithelial cells of the embryo from epithelial cells in the adult under similar conditions, and the example of inflammation has only to be cited for it to be recognised that in extra-uterine life the composition of a mass of tissue by young and rapidly growing connective-tissue cells is an extremely common occurrence. Owing to these difficulties in reference to the use of the terms it is better to dispense with them altogether. Something of the same difficulty pertains to the use of the terms *adult* and *embryonic*, which are frequently employed in connection with the new-growths. The terms epi-, hypo-, and mesoblastic, which are still frequently used in speaking of tumours, even intensify the difficulty. For they introduce terms which tacitly imply the acceptance of views as to the earliest changes of intra-uterine life, which are far from being universally accepted, and which are at the present time certainly not held in the strict manner that was implied when they were introduced. Upon the whole, then, it is better to restrict ourselves to terms which have an anatomical, and therefore a definite, meaning. We shall run no risk of being misunderstood if we describe a tumour as being formed upon the type of epithelial tissue, whether squamous, columnar, or spheroidal, or upon the type of one of the members of the connective-tissue group, whether fibrous tissue, cartilage, or bone. Even this mode of division, however, will not suffice to include all varieties of tumour, for certain of them partake of the characters of both groups ; but it has, at least, the advantages of including the great majority of the new-growths and of not committing us to the acceptance of any theory which we may at any minute be called upon to renounce.

Distinction of the new-growths into malignant and non-malignant is of the greatest importance from the clinical point of view, though from a purely pathological aspect it is not so satisfactory, because it is not unfrequently impossible from a microscopical examination alone to decide whether a tumour is clinically malignant or not. This will be seen to be particularly the case when we come to consider the malignant neoplasms known as sarcomata.

The criteria of malignancy are that the growth tends to return locally after what has apparently been its complete removal, that it progressively invades and destroys the tissues in which it is present, that it leads to the formation in distant parts of the body of secondary tumours which are of like composition with itself, and that, in virtue of these characteristics, it ultimately destroys life. Certain other distinguishing characteristics between the non-malignant and the malignant growths follow as corollaries from the above-mentioned 'criteria.' Thus, a non-malignant tumour is almost always encapsuled, whereas this is not the case with the malignant tumours. This difference partly arises from the characteristic of the malignant growths that they invade the surrounding tissues, and partly from the fact that they increase in size far more rapidly than the non-malignant growths, and therefore do not give the tissues time to react and form a capsule around them. Upon this same characteristic, too, depends the tendency of the malignant growths to recur locally after removal; the fact simply means that the actual limits of the growth extend far beyond those which are evident to sight and touch.

There is a considerable variation in the degree of malignancy even among the members of what are known as the malignant group. Thus, the tumour known as **rodent cancer** or **ulcer** is only locally malignant; it does not tend to form secondary growths elsewhere, and may not cause death for a number of months; on the other hand, the **melanotic** form of sarcoma forms secondary deposits from a very early stage and destroys life rapidly. There is the same difference in rate of growth, though it is not generally demonstrated in so marked a degree, among the non-malignant tumours. A fibroma, for example, so long as it still remains non-malignant, never grows anything but slowly, while a myoma of the uterus may attain a considerable size in a short time.

It has already been said that it is sometimes impossible to distinguish from a microscopical examination whether a given tumour is malignant or not; this is also the case clinically, at times. For, putting on one side the cases in which a doubt exists in the mind of the surgeon which is completely cleared up when a portion of the growth has been subjected to microscopical examination, there is a class of case in which the tumour seems to pass insensibly from the non-malignant into the malignant category. An example of this statement is afforded by the growth known as **recurrent fibroma**. This tumour, which is especially liable to occur in the subcutaneous tissue, appears to be a simple fibroma, it is removed, and the microscope confirms the diagnosis, with, perhaps, the additional information that the growth is somewhat more cellular than is usually the case with the fibromata. After a shorter or longer period the growth recurs locally and is again removed, the microscope on this occasion showing that the number of cells is greater than before. And thus it goes on, becoming more and more cellular, and recurring at shorter and shorter intervals, until at last the histological characters of the growth cannot be distinguished from those of a malignant growth (sarcoma). At what point it ceases to be a non-malignant fibroma, if indeed it was ever such, and becomes a definitely malignant fibro-sarcoma, it is impossible to say.

Numerous other forms of growth show the same tendency to pass from a condition of non-malignancy into a condition of malignancy, but this is only if they are not removed; the recurrent fibroid is the only one that is at all common in which the clinical and microscopical characters are those of a definitely non-malignant growth at its first removal, but in which the subsequent history is that of a locally recurring, and therefore of a malignant, tumour. Owing to these characteristics of the tumour, many authors refuse to include it among the non-malignant growths at all.

In the case of the warts that are so common in childhood about the age of puberty, and which are frequently present in great numbers upon the hands, we have a condition which is in great measure the converse of that which is the case with recurrent fibroma. For there is no doubt that these warts are not malignant in the clinical sense of the term, nor are their histological characters other than those consistent with non-malignancy. Nevertheless there is equally no doubt that one wart frequently becomes the centre of a group which seem to have originated from it, and that, in this respect, they have much in common with the truly malignant growths. So, too, in the rare condition of cystic disease of the antrum, the histological features are such that even a competent histologist unacquainted with this special tumour would hardly hesitate to pronounce it malignant, and yet the growth has no tendency to recur after removal, neither has it any of the other criteria of malignancy.

But after all cases of this description are not those which cause the greatest actual difficulty to the pathologist. The most difficult cases are those in which a diagnosis is required between sarcoma and ordinary granulation tissue on the one hand, and between carcinoma of the breast and simple chronic mastitis on the other. Cases of these kinds require the utmost care because of the immensely important issues involved.

THE ETIOLOGY OF TUMOURS

There is hardly a point in pathology which is less certain than that concerned with the question as to why tumours arise and what is the agent which leads to their appearance. Consistently with this fact the number of theories that have been put forward is commensurately great. We shall not enter into their consideration in detail, but it is necessary to make some reference to those which have attracted the greatest amount of attention.

(1) **The mechanical irritation theory of Virchow.**—According to the view propounded by this authority, the principal factor in the causation of the new-growths is mechanical irritation. Evidence in its support is afforded by the following considerations. Workers in paraffin and tar are liable to suffer from malignant diseases (squamous cell carcinoma) of the arms; chimney-sweeps sometimes suffer from scrotal cancer from the effects of the constant irritation of the soot-begrimed part against the clothes and thighs;[1] a cancer of the lip is apt to develope where the part is irritated by a ragged tooth or by a clay pipe; the ends of nerves in an amputation stump are the especial seats at which one finds tumours of nerves; cancer sometimes develops in the course of an ordinary scar. Facts such as these seem to point in a very distinct way to a relation between the new-growth and the irritation which is certainly present. The great arguments against the view are, first, that a large majority of the new-growths do not occur in situations at which the existence of an actual or an antecedent irritation is recognisable; second, in a vast majority of cases of definite injury there is no subsequent development of a new-growth, and therefore there is a possibility that the cases which have been cited are to be regarded as coincidences, and not as causes and effects; and, third, it practically leaves the entire group of the non-malignant growths without an explanation.

(2) **The theory of embryonic remnants of Cohnheim.**—According to this view we have to look for the beginnings of the new-growths in small groups of cells which are cut off from their sister cells during intra-uterine life; the cells so cut off fail to develop into the tissue which is formed by their sister cells, but lie, so to speak, in a latent condition in the midst of the fully formed tissue. When some stimulus arises which can rouse their latent capacity for growth into action, they commence to proliferate as they were proliferating when they were segregated, and according as they were segregated early or late during embryonic life, so the tumour which they form will have less differentiated or more differentiated characters, and *pari passu* the cells of which it is composed will tend to proliferate (and

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[1] This form of cancer is far less frequently seen at the present day than formerly when it was customary for sweeps to climb the chimneys in pursuance of their occupation.

therefore the tumour itself will tend to grow) more rapidly or less rapidly.

It is impossible here to enter into a discussion of this theory, and to give the arguments by which Cohnheim sought to support it. Shortly, they amount to the facts (1) that we have plentiful evidence, particularly in the case of the generative organs, that cells may be endowed at birth with a capacity for growth which shall not evidence itself till many years later, and in some cases, as with a uterus which never receives the stimulus of an impregnated ovum, not at all; and (2) that the situations at which new growths are most frequently met with are situations at which there has been some complicated process in embryonic life, and are in consequence particularly the positions at which a segregation of a group of cells, such as he supposes, might be expected to occur.

The chief objections to this view are as follows. First, the impossibility of either proving or disproving the existence of embryonic remnants themselves. Second, the fact that new-growths are very infrequent in the brain and the kidney, both of them organs of which the embryological history is very complicated. And, third, the fact that, in attempting to find support for his theory, Cohnheim forced the teratomata into an unnatural position by including them among the true tumours, and denied to certain forms of cancer (e.g. scrotal cancer in chimney-sweeps, cancer on the arms of workers in paraffin and tar) their rightful position among the new-growths.

But though the theory of 'embryonic remnants' does not at the present day command the full acceptance of pathologists with regard to the etiology of all kinds of new-growth, it is allowed on all hands that for certain classes of tumour it affords the best and most plausible explanation. At the present day it is commonly accepted as an explanation for the enchondromata which arise in connection with the osseous portions of long bones, for tumours of the parotid and testis which contain cartilage, for a variety of renal tumour which contains striated muscle fibre, and for some others. For the entire class of teratomata, or dermoid tumours, and for certain kinds of cyst, it affords a highly satisfactory explanation.

(3) **The parasitic theory.**—This theory is in some way an extension of the principles which we have seen to exist in the case of the infective inflammations. According to it the tumour constitutes in reality the product of the reaction of the tissues to an irritant. The parasitic theory is almost entirely, if not

entirely, concerned with the etiology of the malignant new-growths, and amongst these it has been worked at most extensively in the case of the carcinomata. The foundations of the theory rest upon three considerations. First, upon the discovery in certain carcinomata, particularly at the growing edge of some examples of cancer of the mamma, of appearances which have been taken as evidence of the presence of low forms of animal life. In the rabbit's liver we often meet with white nodules in the centres of which oval bodies known as psorosperms are present. These psorosperms are animal parasites belonging to the order of Gregarinidæ, and their resemblance in many respects to the appearances met with in the growing edge of many carcinomata has led to the supposition that in the case of carcinoma the appearance is due to the presence of minute animal parasites of like, though not of identical, nature. Second, it is a fact that we meet with 'cancer houses' and 'cancer localities,' that is, with situations in which cancer seems to be endemic, and to affect persons who come to live in them, much in the same way as persons coming to live in a malarious district contract malaria, and persons sleeping in a room which has held a patient with some infectious disease are liable to contract that disease. Third, the theory has been held to be supported by an assumed analogy between the course of the disease in a patient suffering from sarcoma or carcinoma, and the course of such a definitely infective disease as tuberculosis.

In the case of the carcinomata those authors who uphold the parasitic theory inculpate an animal parasite, with regard to the etiology of the sarcomata they are in the main silent. On the other hand, certain authors have brought forward evidence which they assert is in favour of the view that the sarcomata, or at least some of them, are caused by vegetable parasites, and certain varieties of yeasts have been obtained from sarcomata which, according to their discoverers, lead to the appearance of sarcoma-like tumours in animals into which they have been inoculated in pure culture.

We shall not attempt to give an exhaustive criticism of the two branches of the parasitic theory for the origin of new-growths, but it may be pointed out that, whatever its merits, it leaves the entire group of the non-malignant tumours unexplained. Moreover it is certain that a very large number of competent morbid histologists fail to see in the appearances which the upholders of the theory regard as parasites, anything more than somewhat abnormal arrangements of the young and rapidly growing cells of the tumour; they regard them as 'cell inclusions' and maintain, what is undoubtedly true, that appearances indistinguishable therefrom may be seen in a great variety of rapidly growing tissues which are not carcinomatous. As to the assumed resemblance between the clinical histories of sarcoma and carcinoma, so far as generalisation of the tumours and resemblance to the generalisation of tuberculosis or any other infective disease are concerned, a little careful consideration of the two classes of case is alone necessary to convince one that the resemblance is merely superficial and not real. In the case of the carcinomata, therefore, it must be confessed that the parasitic theory rests upon a very slender foundation.

In the case of the sarcomata the case is somewhat different. In the first place, the histological appearances of the varieties of sarcoma have their parallels in different varieties of granulation tissue, so that it is quite impossible in many instances to determine whether the portion of tissue has been removed from an inflammatory or a sarcomatous focus. From this point of view, therefore, we are, so to speak, prepared to receive the view that the sarcomata, like the majority of the inflammations, and especially those in which the formation of granulation tissue is a prominent feature, depend upon a vegetable irritant, using that expression in the broadest sense. Then, too, we have the positive evidence to which reference has been made above. But of far the greatest importance of all work done in this direction are the experiments of Washbourn and Bellingham Smith. These authors have shown that it is possible, by direct implantation of a portion of a growth found on the generative organs of bull-dogs and bull-bitches, to produce in a terrier a tumour which ulcerates locally, which has the histological appearances of a sarcoma, and which kills the animal with the appearance of secondary growths in the lymphatic glands and in distant organs. That is to say, they prove that the condition in the bull-dog is infective, and, so far as our present knowledge goes, the property of infectivity is bound up with the presence of a micro-organism. It is true that the possibility that the condition in the bull-dog may be inflammatory cannot be excluded, but at all events in this instance, if the condition is really inflammatory, it resembles sarcoma so closely that the suspicion is roused that the two conditions are allied in their fundamental nature. More than this cannot at present be said, but many authors who are sceptical as to the present parasitic theory of cancer are ready to believe that a time will come when the sarcomata are recognised as being dependent upon the action of micro-organisms, and therefore have close relationship with the infective inflammations.

(4) **The growth-liberation theory of Ribbert.**—Ribbert assumes that in a tissue which is neither growing nor degenerating there exists a sort of equilibrium between the various elements composing the entire tissue. This equilibrium, which is composed of all the factors acting on the tissues, he terms the *tissue tension*. So long as this state of equilibrium persists growth does not take place, but until it becomes established; and whenever it becomes disturbed, the inherent power of growth which lies in every cell, and is only restrained by the existence of tissue tension, is set free. This process may affect cells of a single kind or it may affect groups of cells forming a more or less complex system, but directly the cells are freed from the restraint of the tissue tension of the part in which they are situated, they commence to proliferate.

The great advantage of this theory is that it supplies one common reason for all kinds of growth, whether normal or inflammatory, whether constituting hypertrophy or leading to the formation of a tumour. Neither does it exclude other theories as to the origin of the new-growths. It is clear that mechanical irritation will be such a factor as will disturb the normal tissue tension, and it is equally clear that it raises no objection to the supposition that embryonic remnants exist. Neither does it militate against the view that parasites are concerned in the etiology of tumours, for a parasite in the tissues would disturb their normal tension. Practically the only objections to its acceptance are that it is impossible to put it to the test, and that it is so extremely simple. The more we learn about pathology the more we are forced to the conclusion that very simple ‘ explanations ’ are generally wrong.

(5) **The ‘ habit of growth ’ theory of Adami.**—It has recently been insisted on by Adami that any explanation of the tumours must take into consideration all varieties of new-growth, teratomata, non-malignant tumours, and malignant tumours. From a consideration of the characters of cells and of the nuclei of cells that are undergoing multiplication or are exercising function, he decides that we must sharply differentiate between those cells which have the habit of growth and those which have the habit of work. These two functions cannot be exercised by the same cell at the same time, and when a cell which normally possesses the habit of work takes on growth (becomes a ‘ vegetative ’ or ‘ proliferative ’ cell), it first of all reverts to the

type of the vegetative cell. In course of time, owing to an inheritance of acquired characteristics, the descendants of such cells as have parted with function to take on proliferation become capable of proliferation only, and thus give rise to a tumour. Such an alteration in habit will take place whenever a larger amount of nutriment is available for the cell than can be used up in the performance of function, and the longer this obtains the greater the tendency for the cells to persist in the altered direction. Further, according to the stage of cell development in which the habit becomes impressed upon the cell, so do we have the various grades of non-malignant and malignant tumour formation. Lastly, it is clear that a large number of circumstances may determine the necessary alteration in the amount of nutriment presented to the cell, so that in one case the exciting cause may be long-continued mechanical irritation, in another the presence of an embryonic rest, in another the presence of a parasite, in another alteration of the tissue tension, and so on.

General histological characters of the new-growths.—Like the normal tissues of the body, the new-growths consist of cells, with the addition in different degrees of many of those more complex systems of tissue that are produced by cells. In the simplest form of tumour the entire new-growth consists of cells alone. This, however, is really only found in the case of a collection of epidermal cells constituting a *callosity*, a non-malignant formation which hardly comes within the category of the tumours. In all other instances something more is present than the mere cells themselves. It may be only the fibrils of fibrous tissue which are produced by the connective-tissue cells, as in a simple fibroma ; it may be connective tissue, together with blood-vessels, as in the case of the vast majority of tumours ; it may be bone or cartilage, or even unstriated or striated muscle. Sometimes the tumour is composed of a tissue bearing a more or less close resemblance to one of the more complex tissues such as a gland.

But in the case of all tumours there is always something which allows them to be differentiated from a normal tissue. Except in the case of a tumour definitely composed of abnormal lymphatic vessels, the new-growths are unprovided with lymphatics, though, of course, spaces lie between the cells which we may, if we so wish, call lymphatic spaces. And, except in the case of tumours definitely composed of abnormal nerve filaments, the new-growths are unprovided with nerves. With these exceptions the elements entering into the composition of the tumours are identical with those found in normal parts, though they need not be, and most generally are not, strictly typical.

With regard to the last statement the example of a simple fibroma has already been cited. Simple examples are to be found with readiness. Thus a tumour composed of blood-vessels (angeioma) does not consist of normal blood-vessels, whether capillaries or veins, but the irregular spaces in which the blood lies are bounded by walls that bear only a remote resemblance to the walls of capillaries or veins. For the walls consist only of a small amount of fibrous tissue coated on the side towards the blood with a layer of cells suggesting, but certainly not to be mistaken for, an endothelial lining of a blood-vessel. So, too, in the case of a fibro-adenoma of the breast, a tumour which is built up on the type of glandular tissue, we find crypts lined by an epithelium, but the crypts themselves are far more irregular in their arrangement and distribution than is the case with normal breast tissue, and the epithelium lining the crypts, though its arrangement is fairly orderly, has not the same characters as the epithelium lining a normal acinus of the gland.

Amongst the malignant growths this departure from the normal type is still more marked. A sarcoma consists, it is true, of connective-tissue cells, and though we may not be able to distinguish a sarcoma cell from any other young and rapidly growing connective-tissue cell, there is a difference in the arrangement of the blood channels by which the growth is supplied. For even in so young a specimen of connective tissue as early granulation tissue, we find that the blood-vessels are composed of definite elements, the ordinary elements of a capillary, it is true, but in a sarcoma the blood is contained in channels which have no right to be classed as vessels, since they are possessed of nothing approaching to a wall. Amongst the epithelial malignant growths (carcinomata) the same is true. A carcinoma consisting of squamous epithelium shows the existence of a germinating layer, of prickle cells, of a granular layer and of a keratinous layer; but the arrangement is different from that in normal skin and quite disorderly, and the cells of the individual layers have their own particular differences also. Nevertheless the characters of the squamous cell are in no case so far lost that it can be mistaken for a columnar or a spheroidal cell, and the same preservation of type is seen in the carcinomata composed of columnar and of spheroidal cells respectively. The utmost that occurs is that the columnar and the spheroidal varieties of epithelium converge towards an indifferent type which is often spoken of as **transitional** epithelium.

In their capacity of tissues foreign to the normal body the new-growths act as irritants to the tissues in the midst of which they are placed. They therefore lead to an inflammatory reaction on the part of the normal tissues in their immediate neighbourhood. This reaction is commonly a mild one, for the irritant is, in our present acceptation of the term, an aseptic one, and its influence is only gradually manifested. This inflammatory reaction on the part of the tissues around a tumour causes the appearance of a narrow zone of small round cells, partly leucocytes and partly proliferated connective-tissue cells, in advance of the growing edge of the tumour. When the tumour is of very slow growth, as in the case of most of the non-malignant tumours, this inflammatory zone is of small extent and becomes organised into a barrier of newly formed connective tissue which constitutes the capsule of the growth. Under these circumstances the appearance of a zone of small round cells in advance of the tumour becomes lost. But when the growth increases in size more rapidly, as in the case of most of the malignant growths, this advance zone of small round cell is conspicuous.

The changes which are undergone by the cells of the advance zone in the case of the malignant tumours are identical in kind with those occurring in it in the case of the non-malignant, but owing to the different rates at which the two types of tumour increase in size, the ultimate pictures produced are different. It has been said above that the capsule which surrounds a non-malignant tumour is formed at the expense of the cells constituting the zone of reaction, and it is obvious that the capsule which consists of fully formed connective tissue could not have been formed unless the proliferated fibrous-tissue cells had had time to become converted into fibrous tissue. That is to say, the prime factors in the formation of the capsule were that the irritant action of the tumour itself was so slight that it constituted a stimulus, and that the growth of the tumour was sufficiently slow for the encircling zone of proliferated connective-tissue cells to become converted into an encircling zone of fibrous tissue. In the case of the malignant new-growths the conditions are different. The tumour does, it is true, act as a stimulus to the proliferation of connective-tissue cells, but its rate of growth is so rapid that before these newly proliferated connective-tissue cells have had time to form definite fibrous tissue the cells of the tumour have passed beyond their confines. The tumour now causes the appearance of a fresh zone of small round cells, but those which had formed the advanced zone previously continue, if they are not destroyed, to produce fibrous tissue, which by force of circumstances does not encapsule the growth, but lies within its boundaries. Hence in the case of the non-malignant tumours the normal tissues of the body in the immediate neighbourhood of the tumour strive to encapsule the tumour, and succeed, but in the case of the malignant growths the tissues in the neighbourhood are always trying to encapsule the growth, but never succeed. On the contrary, the cells of the tumour always form an irregular zone outside any fibrous tissue which the normal tissues may produce.

Even in the case of the malignant tumours it does not always happen that the centre of the growth consists largely of fibrous tissue. In carcinoma of the breast the condition is certainly present in the majority of cases, so that such tumours are generally of stony hardness in the centre. We may go further and say that, *cæteris paribus*, the oldest portions of any malignant growth show a marked tendency to be denser than portions close to the growing edge, and this is equally true of a primary growth, compared with secondary growths to which the primary growth has given rise. But the statement tacitly implies that no factor shall intervene to prevent the formation of fibrous tissue by the newly proliferated connective-tissue cells. As a matter of fact, it is not uncommon for such a factor to intervene, and then the centre of the growth is as soft as the outlying portions; indeed, it is likely to be softer, for the factor to which reference is made is represented by one or other of the degenerations, as we shall see later.

Effects of a new-growth upon the surrounding tissues.—We have already referred to the immediate effects of the presence of a tumour in a part, and have said that it leads to the appearance of an inflammatory reaction on the part of the tissues in its immediate neighbourhood. But a tumour has other effects than these, and they differ in a considerable degree according as the tumour is malignant or non-malignant.

Where the tumour is non-malignant the normal tissues of the part in which it is situated are displaced by the growth and also undergo a certain amount of pressure atrophy. But displacement and atrophy are the only changes brought about. Moreover the degree of pressure atrophy is not commonly great, and in any case bears a definite ratio to the size of the tumour, varying directly with it. But the case is different with the malignant growths. Displacement occurs, it is true, but atrophy of the normal tissues around the tumour assumes far more considerable proportions. That invasion of the tissues which is a fundamental characteristic of the malignant tumours is the cause of the equally fundamental characteristic that they destroy the tissues in which they lie.

The new-growths also affect the tissues in other ways, and again there is a difference between them. For the non-malignant tumours may, by the pressure which they exert upon surrounding parts, owing to their size or their situation, produce severe or even fatal complications. Thus, a fibro-myoma of the uterus situated upon the posterior wall of the organ may lead to fatal complications by way of the urinary bladder and the kidneys, or by way of the intestinal tract, while a tumour of the same size situated upon the anterior wall is a matter of relatively little importance. And the same may occur in any other case in which the tumour is situated in a region where the pressure it can exert may be expended upon some tissue or passage which is necessary to life.

But in the case of the malignant growths it is different. The malignant growths can act by virtue of the pressure they exert just as much as the non-malignant, and in a large number of cases actually destroy life in part by this means. But, in addition, they act injuriously upon the tissues generally, and at a distance from themselves, so that a rapid loss of flesh on the part of the patient, anæmia, and other signs of severe disease are produced. How they lead to the occurrence of these symptoms it is at present impossible to say. It has been suggested that the tumour, being a tissue which requires a considerable amount of nutrition for its growth, and being, physiologically, outside the body, diverts most of the nutriment absorbed to its own uses, and, in addition, draws upon the normal tissues themselves. It has also been suggested that the malignant tumours throw into the blood stream products of their own metabolism which are toxic to the rest of the tissues. Whether this latter suggestion is true, it is impossible to say, but it is certain that the presence of a malignant new-growth in the body causes it to undergo something more than simple chronic starvation.

Changes undergone by the new-growths.—The new-growths are liable to almost all the degenerative changes that involve other tissues, and to certain of them they are even more prone. Thus fatty degeneration is of frequent occurrence in highly cellular growths like the sarcomata. Mucoid degeneration also frequently occurs and leads to the formation of cysts ; cystic fibro-myomata and cystic sarcomata are almost always produced by the localised mucoid degeneration of masses of cells in the centres of the growth where the blood supply is deficient. Colloid degeneration occurs in the case of carcinomata, particularly those of the alimentary tract and the breast, but it is not of so frequent occurrence among the carcinomata as mucoid degeneration is among the sarcomata. Calcification is common in the case of slowly growing tumours which are ill supplied with blood-vessels; of all varieties of new-growth, fibro-myomata of the uterus are the most liable to this change. In some cases we find the formation of crystals of cholesterin along with some one or other of the liquefactive changes. Thus, a sarcoma of the kidney, which is especially liable to be broken down in the centre as the result of degeneration, will often show the presence of a number of crystals of cholesterin floating upon the surface of the fluid that fills the cyst.

Besides the changes mentioned above, new-growths, and especially malignant new-growths, are liable, when they reach a surface, to undergo a destruction which is commonly called **ulceration**, but which, having no connection with inflammation, is better called **molecular necrosis.** This change, it has already been said, is really nothing more than a variety of gangrene due to deficiency of blood supply, coupled with an abnormal exposure of the cells to injury. A malignant ulcer has a ragged and foul-smelling base, hard everted edges, and shows no tendency to heal.

The non-malignant growths are less liable to the occurrence of degenerative changes in their cells than the malignant. But they are liable to undergo a change of type. That is to say, they are liable to take on the characters of the malignant growths, and thenceforward must be treated as such. This change is of so great importance that it calls for a more detailed description. This will, however, be deferred until we are considering the classification of the new-growths.

Caseation, the hyaline change, and the lardaceous change only affect tumours with great rarity.

CLASSIFICATION OF THE NEW-GROWTHS

At the beginning of this chapter certain broad lines of classification that have been adopted in the case of the new-growths were discussed, and it was then said that the best method of classification is one which depends upon an anatomical basis subject to the great distinction of neoplasms into non-malignant and malignant. If, then, we take the two great divisions, non-malignant and malignant, and subdivide these severally into epithelial and connective-tissue groups, we shall be able to account, in one or other of them, for the great majority of tumours. It will prove of assistance, however, if at the same time we pay some attention to the classification based upon embryological data.

CLASSIFICATION OF NEW-GROWTHS

Type	Origin	Typical and non-malignant	Atypical and malignant
Epithelia	Epiblast	Callosity. Keratoma Papilloma of skin	Carcinoma Squamous Columnar Spheroidal
	Hypoblast	Papilloma of intestine	
Connective tissues	Mesoblast	Fibroma. Myxoma. Lipoma 'False neuroma' Chondroma Osteoma. Exostosis Odontoma Angeioma Capillary Venous Lymphatic Glioma	Sarcoma Round cell Spindle cell Oat cell Irregular cell Myeloid (giant cell) Pigmented (melanotic, chloroma) Alveolar Psammoma Endothelioma
Muscles	Mesoblast	Striated (rhabdo-myoma) Unstriated (leio-myoma)	Sarcoma
Nerves	Mesoblast	Neuroma	Sarcoma
Gland	Secreting (Epiblast, Hypoblast)	Adenoma	Adeno-carcinoma Spheroidal Columnar
	Lymphatic (Mesoblast)	Lymphoma, lymphadenoma	Lympho-sarcoma

The classification here given conveys more than a simple statement of the anatomical variations of the tumours; it also indicates the form of new-growth that will be produced if a non-malignant tumour takes on malignant characters.

It was at one time thought that the tissues were capable of passing from one type into another, so that, for example, a carcinoma was produced by the actual conversion of connective-tissue cells into the epithelial cells which constitute the main element of a true cancer. This idea, which was embodied in the 'theory of metaplasia,' is now given up, and the limits within which a change of type is possible have been greatly contracted. It is allowed that a certain degree of mutability of type obtains amongst the members of one anatomical group, so that in the case of the epithelia we find rapidly growing columnar cells, showing many of the characters of spheroidal epithelium, and columnar epithelium covering a surface which, owing to some pathological condition, has become exposed to irritation and pressure, showing many of the characters of squamous epithelium. But the actual change of the columnar cells into either of the other two types never occurs, and if the special circumstance which leads to the abnormality disappears, the cells again revert to their original characters. We now, therefore, believe that one of the principal laws of cell life is that cells breed true, and that metaplasia, in the original sense of the term, does not take place.

It follows from what has just been said that the characters of a growth will be determined in very large measure by the tissue from which it springs, so that a growth arising in one or other of the connective tissues cannot but belong to this group any more than a tumour springing from an epithelium can help being epithelial. And this is true whether the tumour be non-malignant or malignant. It is also true in cases where a non-malignant tumour becomes malignant, so that a papilloma, which is an epithelial growth, when it becomes malignant, develops into a carcinoma and not into a sarcoma, while a fibroma undergoing malignant transformation becomes converted into a sarcoma and never into a carcinoma.

The rigidity of the rule that cells breed true is even more clearly seen in the case of the epithelial growths themselves. Thus, a papilloma of the skin which is covered by squamous epithelium never becomes converted into a spheroidal carcinoma, but always into a squamous cell carcinoma; whereas a papilloma of the rectum, which is covered by columnar epithelium, always becomes a columnar cell carcinoma if it takes on malignancy, and never any other kind. This character also obtains in the case of secondary nodules of a malignant growth. A squamous cell carcinoma of the lip, for example, if it forms secondary nodules in the liver, forms them out of an epithelium which has the peculiar characters of squamous epithelium, although this type of epithelium is completely absent from the normal liver. It may be that the characters of the primary growth are not reproduced in the secondary growths in every particular. But the differences are small, and may generally be explained by the fact that growth proceeds more rapidly in the secondary nodules than at the focus of the primary disease. For this reason we find that a dense spheroidal cell carcinoma (scirrhus) of the breast leads to the presence of a soft highly cellular cancerous deposit in the lymphatic glands of the axilla; there is a marked difference in the amount of fibrous tissue present in the two situations, but the cells in both are cells of spheroidal epithelium.

In the case of connective-tissue growths the same law holds good, but there is somewhat more variation in type. Thus, a malignant growth arising from the periosteum must of necessity be sarcomatous, but it cannot be decided with the same certainty that it will be an osteo-sarcoma. It may be a large or a small spindle cell sarcoma, it may be composed of large or small round cells, or it may be composed of a mixture of these varieties. In addition, it may be the seat, not of true ossification, but of calcification These differences, however, are not differences in the essential nature of the cells so much as differences dependent upon the rapidity with which they multiply. So we find, as has already been said when referring to the case of recurrent fibroma, that the secondary deposits in a case of a sarcoma tend to show a diminished differentiation, so that the primary growth may be a large spindle cell sarcoma, while the secondary nodules are composed of small spindle, or, it may be, of round cells. With increased rapidity of growth, the tendency to differentiation of the cells composing the growth seems to be diminished. The contrary to this—viz. greater differentiation of the cells in a secondary deposit—is never seen. Thus we never find that a primary fibro-sarcoma gives rise to the appearance of chondro-sarcoma in the secondary deposits, though the contrary is common enough. Neither do we find that a primary small round cell sarcoma is associated with large or small spindle cells, or even with large round cells, in any of the secondary growths to which it may give rise.

The advantage of considering the new-growths from the point of view of the embryological layers from which they are supposed to be developed is more evident in the case of the malignant growths than in that of the non-malignant. For we can say with comparative certainty that, if a tissue has been developed from epiblast or hypoblast, a carcinoma will be produced, and that if it has developed from mesoblast, the malignant new-growth will be sarcomatous. The advantage in this case is that we do not require special classes for growths arising in muscle or in the nerves, but can decide at once that since these forms of tissue are of mesoblastic origin, any malignant new-growth to which they may give rise must be sarcomatous.

We meet, however, with certain difficulties. The kidney, for example, is generally considered to have arisen from the mesoblast, and on this account the malignant tumours of the kidney ought to be sarcomatous. As a matter of fact, in a large number of cases they are sarcomatous, but it is not at all uncommon to meet with malignant tumours of the kidney which are undoubtedly carcinomatous, though the variety of carcinoma present is one which it is not common to find in any other organs than the testis and ovary, organs which, of course, have close developmental relationships with the kidney. A possible exception to the statement just made occurs in the breast, where malignant growths are not uncommonly found that bear many points of resemblance to the carcinomata of the kidney, the testis, and the ovary.

As to the explanation for this peculiarity there is considerable doubt, and some authors evade the difficulty by refusing to speak of the growths in question as carcinomata, but term them 'proliferating cystadenomata.' We must allow that the new-growths of the kidney, testis, and ovary constitute one of the most difficult portions of the whole subject of the tumours, and more will have to be said concerning them later. But it may be mentioned here that the anomalies have been explained by some authors on the supposition that, in the development of these organs, portions of overlying epiblastic or hypoblastic layers have been included. The fact that tumours of the testis are sometimes found to contain cartilage is an argument in support of this view; for it is quite possible that portions of embryonic cartilage may be included in the primitive sex-gland when we consider how close that organ is placed to the cartilage forming the proto-vertebræ.

Corresponding to the belief of embryologists that endothelium is of mesoblastic origin, malignant growths formed of this variety of cell are placed along with the sarcomata. In histological features, however, they offer so many points of contrast with the common sarcomata that they are usually designated by the special term. From their histological characters alone we should be inclined to include the endotheliomata among the carcinomata. Reference will be made to these points later.

Before passing to the consideration of the special forms of new-growth in detail, a word must be said with regard to the use of the term 'adeno-carcinoma.' The term is more frequently employed on the Continent, and particularly in Germany, than it is in this country. As a matter of fact, there is no great argument to be brought forward for its retention, and it was only inserted in the classification on page 152 for the sake of indicating that when a secreting gland tissue becomes the seat of a malignant tumour, that tumour maintains a general resemblance in its arrangement to gland tissue. We might equally well have used the term 'carcinoma' alone, qualifying it according as the constituent cells are of the spheroidal or of the columnar type. A further reason existed in the fact that it was wished to bring the malignant new-growths of secreting gland tissue into contrast with the malignant growths arising in lymphatic gland tissue (lympho-sarcoma). In this instance the use of the sole term 'sarcoma' would be unadvisable, for, as we shall see, a lympho-sarcoma is not merely a sarcoma in a lymphatic gland.

SECTION VIII

THE NEW-GROWTHS OR NEOPLASMS—continued

THE NON-MALIGNANT TUMOURS

In considering the tumours in detail it will be convenient to divide them into the non-malignant and the malignant classes. Not only are there well-marked differences between the histological characters of the two groups, but also, in this way, the clinical distinctions between them will be better kept before the mind. Subject to this main division, we shall describe the growths according to their chief histological features.

(1) THE NON-MALIGNANT EPITHELIAL TUMOURS

(*a*) **Callosity.**—A callosity is one of the simplest of new-growths. Indeed, from a clinical point of view it can hardly be included among the tumours at all. It consists merely of a localised collection of epidermal cells, and in reality may be looked upon as a localised exaggeration of the normal conversion of the prickle cells of the epidermis into cells of the horny layers. It is the result of an excessive stimulation of the germinating layer of the epidermis combined with the lack of a corresponding removal of the most superficial keratinous layers. These changes are produced as the result of pressure intermittently applied, and consequently callosities are chiefly met with on the flexor surfaces of the hands and feet, but they may be present over the olecranon and the ligamentum patellæ. As a rule, callosities cause no trouble, but occasionally they cause so much pain that their removal is necessary. This principally occurs in the case of callosities on the soles of the feet. In addition to the features that have been mentioned, the inter-papillary processes of epidermis beneath a callosity are commonly found to encroach more deeply than normal into the corium; this appearance is one very commonly seen in epidermis bordering upon a focus of irritation. Callosities are often erroneously termed 'corns,' but, as will be seen later, the histological appearances of a corn are somewhat different.

(*b*) **Keratoma.**—A keratoma or cutaneous horn is a localised accumulation of the horny layers of the epidermis like a callosity, but in the case of a keratoma the focus at which the epidermal accumulation takes place is smaller, while the actual accumulation of cells and the density which they attain are far greater. A cutaneous horn may therefore reach to a considerable length. Horns generally exhibit a more or less regular spiral twist. The regions which they affect are not those upon which callosities are found, nor does pressure play a part in their formation. As a rule, they are met with upon the face or the scalp. Beneath a horn the papillæ are generally somewhat lengthened and hypertrophied. Horns not infrequently arise in connection with cutaneous tumours involving the sebaceous glands, but they may arise from a corn, a scar, or even from normal skin. They are not of very frequent occurrence.

(*c*) **Papilloma.**—This form of tumour consists in a hypertrophy of the papillæ of the true skin, together with an overgrowth of the epidermal or epithelial layers that cover them. The change is a localised one, so that the tumour projects from the surface of the region in which it is situated. The growth is often dendritic, from the fact that the papillæ of which it is composed become branched. The hypertrophied papillæ themselves carry nerves and blood-vessels, and are therefore in their essential characters like normal papillæ. The epithelium by which they are covered may be either of the squamous or of the columnar variety, according to the situation from which they spring, and the actual amount of epithelium covering the elongated papillæ varies to a considerable degree. This difference in the amount of investing epithelium is a matter of importance; for, since the subjacent papillæ contain blood-vessels, the tendency for the papilloma to bleed on injury will be correspondingly modified. Papillomata of the bladder, for example, are excessively prone to bleed, and this is partly due to the fact that the papillæ are only covered by a few layers of cells, and partly to the fact that the papillæ themselves are very delicate and of inordinate length. When a papilloma occurs on the cutaneous surface it is frequently termed a **wart.** A **corn** is really a specialised form of papilloma upon which a callosity has been superposed. It results from the combined effects of superficial and concentric pressure. The superficial pressure leads to the formation of a callosity, and the concentric pressure causes the thickened layers of epidermis to become depressed at the centre and press upon the hypertrophied papillæ that lie beneath them ; this seat of depression constitutes the 'core' of the corn, and over it there is a collection of dense epidermal scales, which, pressing upon the nerve-endings in the papillæ, cause the pain by which a corn is characterised.

In the case of certain forms of cyst, papillary outgrowths from the wall of the cyst into its cavity are present. These papillary cysts are chiefly found in connection with the ovary ; the epithelium lining the cyst and covering the papillary outgrowths is columnar in type, but the cells are often less elongated than those, for example, which cover the intestinal villi. In the case of certain forms of carcinoma, particularly those which are composed of columnar epithelium, there is a tendency to the formation of cysts with the presence of intra-cystic papillary outgrowths from the cyst-wall. A typical example of this form of carcinoma (often termed 'villous') is afforded by the so-called **duct carcinoma** of the

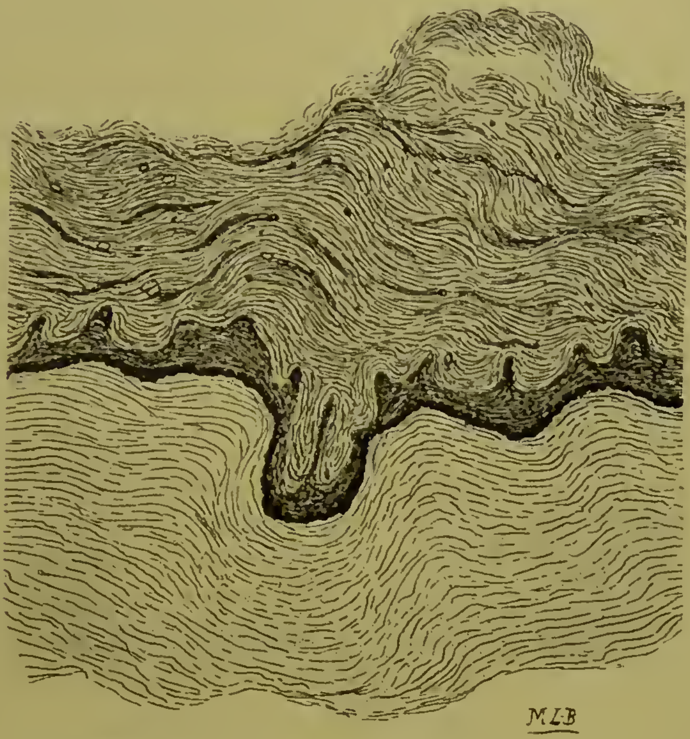

Fig. 29.—Section of a Corn. × 60.

Below are many layers of thickened keratinous epidermis, into which penetrate two papillæ: the remaining papillæ of the portion of skin are flattened and atrophied. Above there is normal loose subcutaneous tissue of the corium.

breast. In the kidney, too, we often find that carcinomata, when present, are columnar cell and villous.

By some authors the papillomata are classed among the fibromata, and it is said that the fibroma has become papillary. To this method of stating the case there is one great objection, viz. that when a papilloma takes on malignancy it becomes a carcinoma. Upon the view that it is a fibroma it should become a sarcoma. For this reason it is better to look upon the papillomata as epithelial tumours. From this aspect, we lose sight of the fact that there is a new formation of fibrous tissue in the formation of every papilloma, it is true, but on the other view the fact that there is a new formation of epithelium is equally ignored.

The principal situations in which papillomata are found are the skin, the intestine, and the larynx, together with the interiors of some kinds of cyst. Much less commonly they are found in the bladder, and they have been found in the gall-bladder and the stomach: indeed they may form upon any surface of the body, whether external or internal.

Sometimes the connection between the presence of papillomata and mechanical irritation is very evident. Examples of this statement are to be found in the presence of condylomata about the anus in cases of syphilis, and the formation of warts about the orifice of the urethra in cases of gonorrhœa. There is evidence, too, that in certain instances infectivity is a property of the papillomata. In the cases of condylomata and gonorrhœal warts the question is uncertain, as the infection may be conveyed by a portion of the original virus which is attached to the papilloma. But there is no doubt that the warts which are so often seen on the hands of schoolboys are infective in the sense that they may be produced on the hands of another boy by direct inoculation of blood taken from a wart. Neither is there doubt that, if a cyst of the ovary which contains intra-cystic papillary growths ruptures into the peritoneal cavity, portions of the papillomata become widely disseminated throughout that cavity, and, being engrafted upon its endothelial lining, survive, grow, and ultimately lead to the formation of intra-peritoneal papillomata.

(2) THE NON-MALIGNANT CONNECTIVE-TISSUE TUMOURS

(*a*) **Fibroma.**—The fibroma is a non-malignant tumour built up of tissue which in its essence is fibrous tissue, though it shows numerous points of difference from normal fibrous tissue. The chief distinction between a fibroma and normal fibrous tissue is one of arrangement of the constituent fibrils. In normal fibrous tissue there is a certain 'waviness,' it is true, but the general trend of the fibrils is clear and unmistakable; but in the fibroma there is no evidence of arrangement, and though sinuosity of the direction of the fibrils is a characteristic, there is a tendency to the formation of whorls, in the centres of which are frequently found the cut surfaces of bundles of fibres running in a direction at right angles to the plane of the section. There is, too, in the fibroma, a density that is not found in the densest of normal fibrous tissue, while the fibrous-tissue cells are correspondingly compressed and irregular. Rarely, even in a scar, do we find the connective tissue so dense as in a fibroma, and in the majority of scars there is not that excessive tendency to the formation of whorls. It must be confessed, however, that from a mere section alone it would generally be impossible to decide with certainty whether the tissue had come from a fibroma or a cicatrix. Nothing more could be said than that the tissue consisted of dense and irregular fibrous tissue.

The actual tissue of a fibroma carries but few blood-vessels; such as are present are situated immediately beneath the surface. It is true that fibromata in certain situations, and particularly when present within the uterus or the cervix, give rise to copious bleeding; but the blood comes from the congested mucous or other surface which covers the fibroma, and not from the fibroma itself. The number of cells in a fibroma varies very considerably. In a dense fibroma such as has been described above, cells are scanty, but in some instances they are so numerous that the growth merits the name of a fibro-sarcoma rather than that of a fibroma.

When a fibroma is situated close to a surface, whether cutaneous or mucous, it has a tendency to become pendulous. It is then termed a **polypus**. All polypi are not fibromata, however; this is the case, for example, with leio-myomata of the uterus, which become polypoid, and pendulous adenomata of the intestine. Nevertheless, fibrous tissue enters largely into the composition of most polypi. A polypus may be attached to its base by a broad or a narrow pedicle, but in any case the nutrition of the growth is carried out by blood-vessels which reach it along the pedicle. A good example of pendulous fibromata is afforded by the cutaneous condition known as **molluscum fibrosum**, in which numerous pedunculated fibromata originally formed in the corium are present on the surface of the body. Uterine polypi are usually fibromata, though, as has already been said, in some instances they are pendulous sub-mucous leio-myomata. (See also p. 164.)

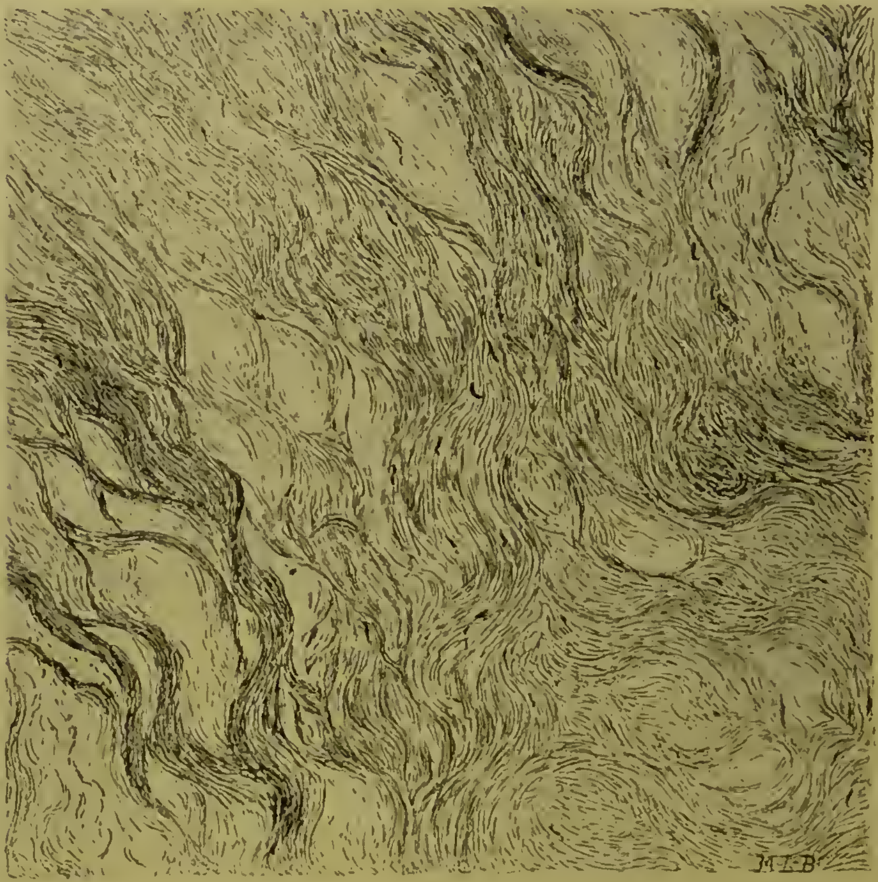

FIG. 30.—SECTION OF FIBROMA. × 60.

The growth was very dense and showed interlacing strands of fully formed fibrous tissue, with very few connective-tissue nuclei. Note the whorl-like arrangement of the fibrous tissue.

(*b*) **Myxoma.**—The type of tissue upon which the myxoma is built is best seen in the Whartonian jelly of the umbilical cord. Strictly speaking, myxomatous tissue is only a somewhat specialised variety of fibrous tissue. It consists of a delicate meshwork of fibrils at the nodes of which are cells with a fair amount of protoplasm and a darkly staining nucleus. The body of the cell is branched, and the branches anastomose to form the delicate connective-tissue network that pervades the tissue.

Between the fibres constituting the meshwork is a semi-solid substance which principally consists of mucin, and which is produced by the myxomatous degeneration of the connective-tissue cells and the fibrils formed by them.

To see fully the structure of a myxoma, it is necessary to examine the tissue in some medium which does not abstract water, for the mucoid substance present contains so considerable an amount of water that when it is abstracted the entire picture is altered. For then the mucin is precipitated and the granular substance which is everywhere present between the connective-tissue fibrils completely alters the appearance of the section. At the same time shrinkage is considerable. The best plan is to harden the myxoma in 5 per cent. formalin and then cut it after freezing; stain the sections with some one of the logwood derivatives, and mount in Farrant's medium. If this course be taken, the features that have been described above will easily be made out.

Myxoma are not merely fibromata that have undergone mucoid degeneration; indeed, fibromata as such do not commonly undergo this or any other form of degeneration, though they not infrequently become œdematous in certain situations. On the contrary, a myxoma starts as such and maintains its character to the end. It must, however, be noted that other forms of connective-tissue tumours, and particularly the sarcomata, are apt to undergo mucoid degeneration, and then we meet with the variety of growth known as a myxo-sarcoma.

The commonest seat for the occurrence of myxomata is undoubtedly the subcutaneous tissue, and here they may form tumours of considerable size. In the museum of St. George's Hospital is a portion of one which weighed more than ten pounds, but this is exceptional.[1] They also occur in connection with the periosteum and in the medullary cavities of the long bones.

Most commonly myxomata are present in combination with some other form of connective tissue, so that we meet with myxo-lipomata, fibro-myxomata, and (in the case of tumours of the parotid gland) chondro-myxomata. In addition to the occurrence of mucoid degeneration amongst the sarcomata, we also meet with definite myxo-sarcomatous tumours.

While dealing with the myxoma it will be convenient to refer to certain growths that are very commonly mistaken for myxomata, viz. œdematous fibromata. In the nose it is often found that the mucous membrane covering the turbinate bones has become polypoid in places. These polypi are in reality overgrowths of the sub-mucous connective tissue which have become œdematous. Hence we find that they are covered by a ciliated epithelium, and that the connective tissue of which they are principally composed shows the presence of numerous spaces, or even cysts, which are filled with a watery fluid. The macroscopic appearance of such a growth is very similar to that of myxomatous tissue, and, no doubt, a certain amount of true myxomatous tissue is often present. Another situation in which œdematous fibromata are often found is the cervix uteri; they here form the so-called **mucous polypus**. In many instances the growths lie on the border-line between inflammation and the true tumours. That is to say, they are often found when the tissue from which they spring has been the seat of a chronic inflammation; but, on the other hand, they often make their appearance in the absence of any such inflammation. 'Mucous polypi' of the intestine are generally characterised by the presence of a number of enlarged

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[1] The patient died of myxo-sarcoma involving the entire pelvis.

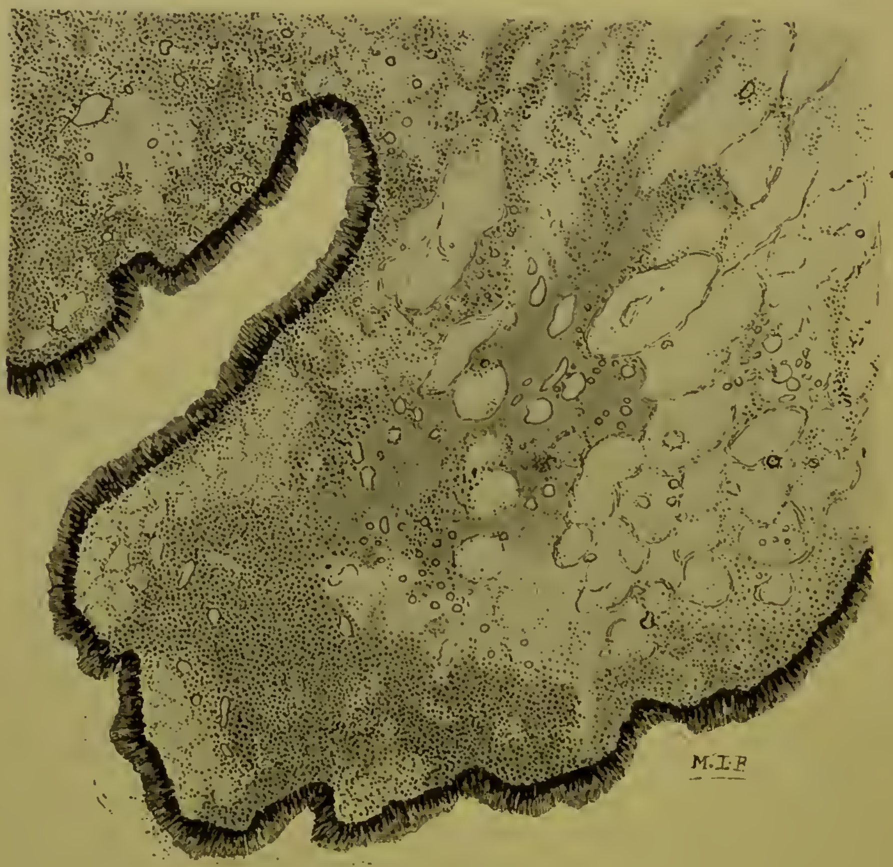

FIG. 31.—SECTION OF A NASAL POLYPUS. × 60.

The growth is a partly œdematous, partly myxomatous, fibroma covered with a beautiful layer of columnar cells. In the myxomatous portions, which stain more deeply, are numerous leucocytes. Very few blood-vessels, and those of small size, are visible.

and sometimes tortuous and branched, tubular glands, and the amount of fibrous tissue which enters into their composition is small. They are therefore neither myxomata nor œdematous fibromata, but are pendulous adenomata.

(*c*) **Lipoma.**—The lipoma is composed of adipose tissue similar, in its histological characters, to the normal adipose tissue of the body. It consists, therefore, of connective-tissue fibrils and cells, the protoplasm of the cells being replaced by fat globules, and the nuclei being compressed at the side of the cell. The amount of fibrous tissue present in a lipoma varies very considerably, and the actual density of the tumour varies correspondingly. In some cases the growth is so soft that it almost feels as if it were a cyst with fluid contents, in others it is taken for a fibroma, and the fact that the tumour contains fatty tissue is only recognised when it is examined microscopically. The fibrous tissue in a lipoma forms trabeculæ throughout the growth, dividing it into portions of unequal size.

Lipomata are not always so circumscribed as to constitute a tumour in the ordinary sense of the term. Sometimes they are *diffuse*, and then the margins of the growth merge gradually into the surrounding tissues. Sometimes, too, they are spread over the whole body, with the result that the patient is said to suffer from obesity; the 'fat women' of fairs are subjects of advanced diffuse lipoma. Apart from this consideration, however, lipomata may reach a great size, ten or more pounds in weight not being very uncommon. As a rule, though, they occur in situations in which their existence is evident to the patient, and, advice being sought, they are removed by the surgeon before they have attained any considerable size.

Occasionally, lipomata become pendulous. This is a more or less normal condition of the lipomata which we call appendices epiploicæ, but sometimes these appendices become more pendulous than usual, and the pendicle may actually be separated, with the result that the appendix epiploica is set free into the peritoneal cavity. It may then contract a fresh attachment, as for example to the capsule of the liver, and excavate a small pit in the substance of the organ, in which it rests. In other instances, the depression is made, but the detached appendix does not contract fresh adhesion. Formations of this kind are not very rarely seen on the convex surface of the liver. In the same way detached lipomata may be found in the cavities of joints, the seat of their original formation having been the synovial fringes. Lipomata of the subcutaneous tissue not infrequently become somewhat pendulous, but their bases are commonly so broad that they do not often become definitely polypoid. Still less do they tend to become detached.

By far the commonest situation in which lipomata are found is the subcutaneous tissue. Even here all parts are not equally prone to their occurrence, for they are usually seen in the fatty subcutaneous tissue of the lumbar, the gluteal, and the scapular regions. From what has been said, it is clear that the lipomata are generally homologous. They are occasionally found, however, in situations from which fat is normally absent. Thus, several instances have been recorded of lipomata of the kidney, and in one case the tumour weighed three pounds and called for surgical treatment. More commonly they are about the size of large peas or beans. So, too, they have been discovered in the sub-mucous coat of the stomach, on the surfaces of bones, in the brain, &c., but in these situations they constitute pathological curiosities, and do not call for further remark here.

Lipomata, like other tumours of the connective-tissue series, may take on malignant characters. They then become sarcomata, but a portion of the original fatty nature still persists, so that they form a composite growth. Further, it is principally lipomata into the composition of which a large amount of fibrous tissue enters that are apt to become malignant, so that the resulting growth is a fibro-lipo-sarcoma. Like other sarcomata, they may undergo further and degenerative changes—in particular, the myxomatous degeneration.

(*d*) **Chondroma.**—In this class are placed tumours composed of cartilage. In most instances the cartilage is of the hyaline variety, but fibro-cartilage may constitute the bulk of the growth. In any case the tissue of the tumour is surrounded by a thin layer of ordinary connective tissue which forms a kind of perichondrium, and is traversed by connective-tissue trabeculæ which carry the nutrient blood-vessels. The cartilage may be highly cellular or cells may be few; as a rule, these different characters are to be met with in different portions of the same growth.

The chondromata are divided into two classes according as they arise from cartilage, or from bone, or other tissue. Cartilaginous tumours arising from cartilage are termed **ecchondromata** or **ecchondroses**, to distinguish them from the **enchondromata** which are heterologous. Ecchondroses are of small importance, and are generally found as small tumours arising from the cartilages of the nasal septum, the larynx, or the ribs. The enchondromata are principally found in connection with the long bones, and especially the phalanges of the hands and feet. It is important to note, however, that the terminal phalanx is always exempt. Tumours of the parotid and of the testis, and occasionally those of the kidney, are apt to be partly enchondromatous ; in the case of the parotid this is the rule, though the actual amount of cartilage present differs considerably in different tumours.

Enchondromata are usually lobulated tumours, frequently multiple, and the individual tumours of a group vary much in size. When they are present in connection with the long bones, they generally arise from the immediate neighbourhood of the epiphysial line, and then they may originate either within the medullary cavity or in connection with the periosteum. It is commoner for the origin to be endosteal, and then the tumour is not recognised at first, but only when it has thinned and expanded the shaft of the bone. Corresponding with this mode of origin, enchondromata are generally invested with a thin layer of bone, but when they have reached any considerable size the shell of bone is wanting, owing to its own disappearance (and the disappearance of the periosteum) as the result of pressure atrophy. Enchondromata arising from the periosteum are rare.

The chondromata are very apt to undergo degenerative metamorphoses. In particular they are liable to become myxomatous in places and to produce, in this way, composite growths. Although they are, as such, non-malignant, they sometimes take on malignancy, and lead to the formation of chondro-sarcomata. It is in the case of chondro-sarcomata that we most commonly meet with degenerative processes. When a chondroma becomes sarcomatous it forms secondary growths, and these usually manifest the presence of cartilage, though they may exist in such a tissue as the lung. When the chondro-sarcoma is highly cellular, and therefore highly malignant, cartilage may be absent from the metastases.

Chondromata are most frequently seen at an age when cartilage, and the changes in cartilage, are especially active. Hence they chiefly affect young persons about the age of puberty.

(*e*) **Osteoma.**—An osteoma is a tumour composed of bone, but it must clearly be recognised that all excessive formations of bone are not osteomata, otherwise we should have to include the callus formed during the repair of a fracture in the class. Neither are all excessive formations of bone, with the exception of callus, to be included among the osteomata, for certain of them lie on the border line between the true tumour and hypertrophy. Of this kind is the condition known as **hyperostosis**, which consists in a diffuse, widespread increase in size of a bone. So, too, the bony outgrowths from the long bones in the neighbourhood of their articulations, and known as **osteophytes,** are not osteomata in the stricter sense of the term, for they are commonly associated with an atrophy of the bone in their immediate neighbourhood, and perhaps also with chronic inflammatory processes. On the other hand, outgrowths from the bones which only differ from osteophytes in their greater size and in the fact that their origin is not known to have any particular antecedent condition associated with it (exostoses), are justly included among the osteomata, although they are given a different name.

The intimate structure of the osteomata corresponds to the two kinds of bone found in the cancellous portions and the shaft of a long bone. Hence we meet with spongy osteomata in which the amount of bone is small, the spaces between the bony trabeculæ large and irregular, the amount of medulla great, and the vascularity correspondingly considerable; and we also meet with osteomata of ivory hardness in which the bone is dense, the medullary spaces extremely small, and the amount of medulla and the vascularity inconspicuous. To osteomata of the former kind the term **spongy** or **cancellous exostoses** is often applied, while for those of the latter kind the name **ivory exostoses** is reserved.

In the case of the teeth osteomata are formed occasionally; they are then usually termed **odontomata**. Some authors reserve this name for tumours which consist of dentine, and speak of tumours which are composed of cement as **dental osteomata.** Tumours formed of dentine result from a hyperplasia of the pulp during formation of the tooth. Odontomata are of extreme hardness and are often tuberculated. They are usually small, but occasionally they are as large as a walnut.

Osteomata may be either solitary or multiple, and multiplicity is by no means an uncommon condition. They usually arise from the periosteal surface of the bones, but enostoses are not unknown. They are most commonly found on the bones of the skull, both on its external and on its internal aspect, on the long bones of the extremities, and on the bones of the pelvis. Ivory exostoses are rarely found in any other situation than the skull.

Osteomata may be formed with or without the existence of an intervening cartilaginous stage. When the latter is the case they are sometimes known as fibrous osteomata. In the majority of cases they arise directly from the periosteum, and then they are formed, like normal bone, through the agency of osteoblasts. Sometimes, however, we meet with a condition which may fairly be called a metaplasia; for in the case of the exostoses, which form in the adductor muscles at their insertion into the femur in persons who ride horseback, and in other similar instances, bone is formed in the tendinous portion of the muscle—a tissue, that is, which does not normally form bone. In the very rare disease known as **myositis ossificans**, the existence of metaplasia is more marked. For in the case of 'rider's bone' there is a possibility that the newly formed bone may have been produced by the periosteum at the point of insertion of the muscle and not from the tendon at all, but in the case of myositis ossificans the bone, which is true bone with Haversian canals and other characteristics of bone, is actually formed in the inter-muscular connective tissue in the centre of the muscles and far away from all periosteal tissue. In this disease the muscles of the back are particularly liable to be affected.

(*f*) **Angeioma.**—The angeiomata are new formations of tissue corresponding to either blood-vessels or lymphatics. In the former case they are termed **hæmangeiomata**, but usually they are spoken of as angeiomata without any prefix; in the latter case they are termed **lymphangeiomata**, but special names have been given to lymphatic tumours when they possess certain characteristics as to histological structure or to situation. A hæmangeioma or a lymphangeioma does not always form a tumour in the etymological sense of the word, for it is often a flat growth which does not project beyond the surface of the skin or other part in which it is present.

Hæmangeiomata may be either capillary or venous, and are often termed **nævi**. Angeiomata composed of vessels that have close affinities with arteries, and, indeed, often spring from arteries, are known, but they are unfortunately called **aneurysmal varices**; they will be described along with the pathological conditions of arteries.

As their name implies, capillary nævi are composed of capillary blood-vessels. But the capillaries of which they consist are very different from normal capillaries. Their walls are thicker and approach somewhat in appearance to the walls of arterioles, consisting as they do of a number of layers of newly formed connective tissue with many cells, and being lined by a well-marked layer of endothelial cells. Often, too, the endothelial cells proliferate and appear to become converted into a tissue which is similar to ordinary connective tissue. If a capillary nævus is full of blood when microscopic sections are made of it, the character of the growth is evident, for the appearance is given of a closely packed congeries of small blood-vessels filled with blood. But in many instances the firmness of the walls, and the fact that they are composed of fibrous tissue, which easily contracts and expels the blood from the vessels, causes the section to appear more like a section of a sweat gland than of a vascular tumour. Sometimes, indeed, the walls are so closely approximated, and the amount of blood present is so small, that the section appears as if it had been prepared from a solid tumour and not from one which had liquid contents during life.

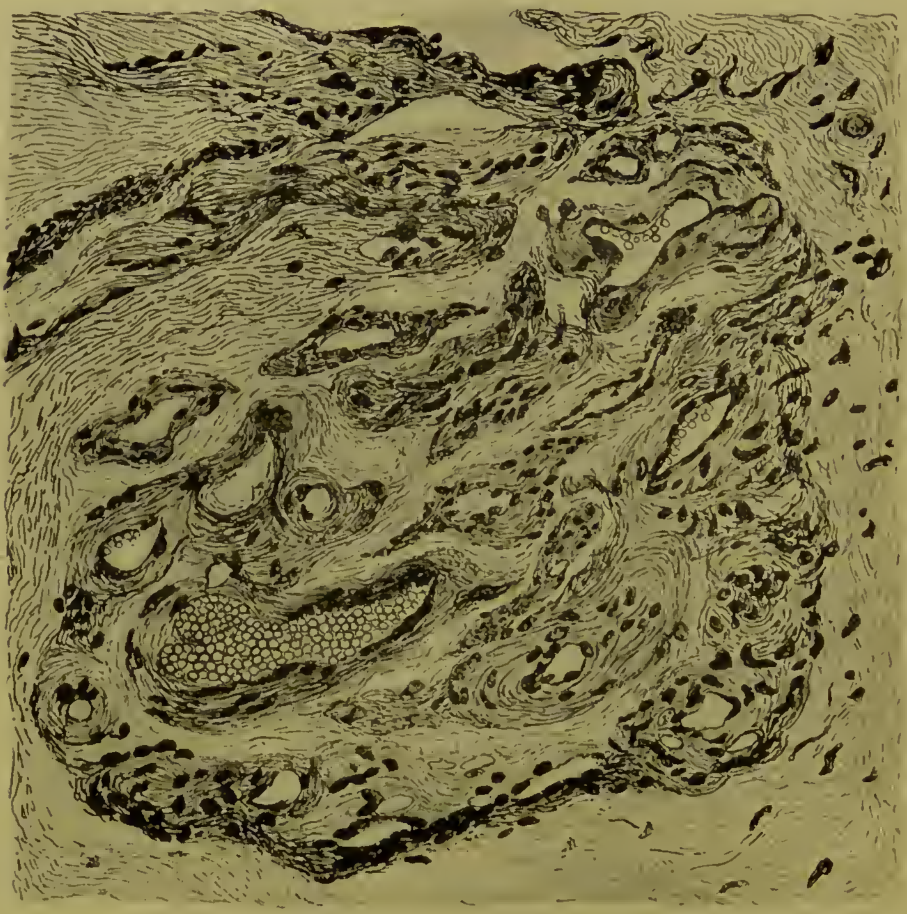

Fig. 32.—Section of a Capillary Angeioma. × 420.

The vessels are of small size and very tortuous; they are lined by endothelioid cells, of which the elongated nuclei are visible, and are surrounded by thick walls of fibrous tissue.

Capillary nævi are congenital tumours, and show themselves as flat or slightly raised patches upon the skin, of an intensely bright red or deep purple colour from the blood which they contain. They may be found on any part of the body, but the face and head are their usual situations. As a rule they are sharply defined from the healthy skin which surrounds them, but sometimes they shade gradually into it. They have a special tendency to be formed at situations at which, in embryonic life, there was a space which was ultimately covered by converging layers of the epidermis. Capillary angeiomata are very apt to increase in size by extension of their edges, and such increase may take place with great rapidity. Hence it is always necessary to remove them when they commence to grow, in spite of the fact that, in themselves, they are non-malignant growths.

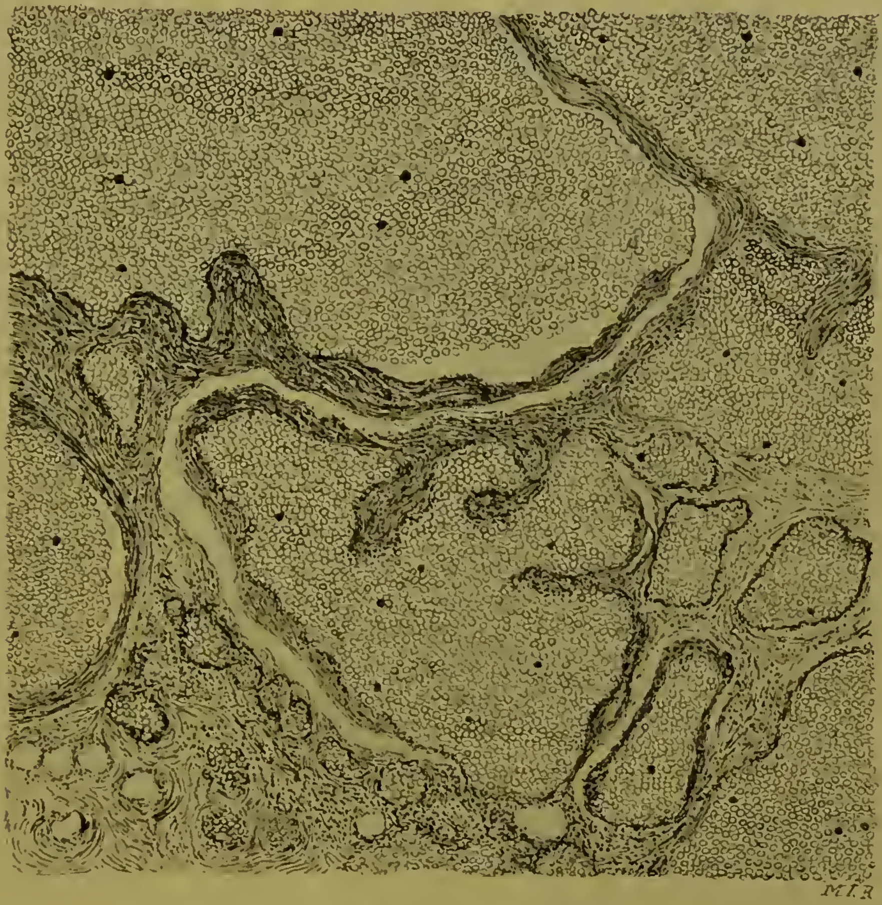

Fig. 33.—Section of Venous Angeioma. × 60.

The blood spaces are large, separated from one another by a small quantity of fibrous tissue, and lined by a layer of endothelial cells. They are filled with red blood corpuscles, amongst which are a few leucocytes.

Venous nævi are built up of a tissue which is very like that composing the corpus cavernosum of the penis, and for this reason they are often called cavernous nævi. They consist of a number of intercommunicating blood spaces the walls of which are thin and have more resemblance to those of capillaries than to those of veins. The walls are composed of a thin layer of fully formed connective tissue containing a small number of cells, and lined on the surfaces towards the blood by a beautiful layer of flattened cells. The spaces themselves are most irregular in size and shape; in microscopic sections they are usually more or less polygonal, but in the normal state they are probably round or oval.

Cavernous angeiomata are found upon any part of the surface of the body, but especially on the face and head, where they form slightly raised swellings which either do not differ at all in colour from the surrounding skin or are of a purplish hue. But they are also found in internal parts, of which the liver is by far the most common, though they have been described as occurring elsewhere. Sometimes they are enclosed by a definite capsule formed at the expense of the tissues in which they are present, but generally they gradually merge into the surrounding tissues without the existence of a capsule.

Cavernous angeiomata are probably not congenital, but they form early in life and may attain to a considerable size. Thus a cavernous angeioma of the face may form an irregular bluish tumour which perhaps involves the entire cheek or side of the face. In the liver they form irregularly quadrilateral masses, which usually reach up to the surface of the organ, but rarely project much above it. They are darker in colour than the surrounding tissue, and on section are seen to be composed of a plexiform tissue between the meshes of which there is blood. They are usually of small size, rarely exceeding that of a walnut, and do not give rise to symptoms.

As in the case of capillary, so in that of cavernous, nævi, the vessels of which the tumour is composed consist in part of dilated pre-existing blood-vessels, but in the main of vessels newly formed and of a somewhat different composition from that of normal veins, as has already been indicated.

Lymphangeiomata are tumours consisting of dilated lymphatics, and the actual composition of their walls does not differ in any considerable degree from the composition of the walls of normal lymphatics. Two varieties of lymphangeioma are described, the **cavernous** and the **cystic**. In addition, a condition is known which is termed **lymphangeiectasis** and in which the normal lymphatics are greatly dilated owing to an obstruction in the thoracic duct, but this hardly comes under the definition of a tumour.

Cavernous lymphangeiomata are of rare occurrence, but they appear to be the essential factor in the formation of the conditions known as **macroglossia** and **macrocheilia**, in which the tongue and the lips, respectively, are of abnormally large size. Cystic lymphangeiomata are chiefly found in the subcutaneous tissue, and generally in that of the neck; they are often termed **hygromata**. The spaces in a lymphangeioma are filled with a fluid which is generally clear and watery, but sometimes it is milky. Lymphangeiomata of all kinds are rare forms of tumour.

(*g*) **Glioma.**—Somewhat separated from the rest of the connective-tissue growths are those tumours which consist of an agglomeration of cells and fibres the prototype of which is to be found in the supporting structure of the nervous elements of the brain and spinal cord. The gliomata consist, like the normal neuroglia, of cells with a very small amount of protoplasm and a number of delicate fibrils which branch and interlace in all directions. Their nucleus is large, both actually and relatively to the cytoplasm, it stains somewhat deeply with ordinary dyes, is round or oval in shape, and often two or three nuclei are visible in one cell of the glioma.

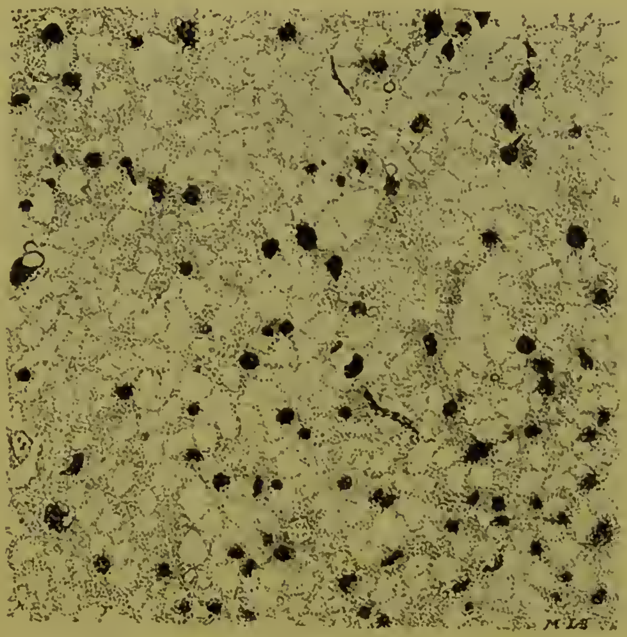

FIG. 34.—SECTION OF GLIOMA. × 420.

The figure shows the large round nuclei of cells with a delicate granular interlacing meshwork between. The latter represents in part the protoplasmic bodies of the cells themselves precipitated by hardening and staining reagents.

The tumours that are formed of such elements as have been described in the last paragraph are only found in those situations in which neuroglia is normally present. Hence the gliomata are tumours of the brain, the spinal cord, and the retina. Even in these regions they are decidedly rare forms of new-growth. In the case of the retina they are apt to become sarcomatous.

The gliomata are commonly soft semi-translucent tumours of a greyish colour which gradually shade off into the normal tissue which surrounds them. They are consequently difficult to recognise until the microscope has been resorted to. In other cases the colour is pinkish or even dark red. Under these circumstances the tumour is traversed by a number of large vessels carrying blood. The tumours are very liable to undergo degenerative changes, so that they may become fatty, or may soften in the centre and become cystic. True nerve cells do not enter into their composition, but the number of neuroglia cells present varies considerably in different cases; in one the tumour may consist almost entirely of fibrils, in another fibrils may be few and cells may predominate largely.

Though true nervous elements do not enter into the composition of the glioma, a variety of tumour is described by some authors which is called a **ganglionic neuroglioma**. It consists of the elements of an ordinary glioma with the addition of true ganglionic cells and nerve fibres. It is difficult to account for the presence of the ganglionic cells in these tumours, but we shall not stop to consider the question, as the tumours themselves are excessively rare.

(3) THE NON-MALIGNANT TUMOURS COMPOSED OF MUSCULAR TISSUE

(*a*) **Rhabdomyoma.**—Tumours composed of nothing but striated muscle fibres are practically unknown, and even tumours into the composition of which striated muscle fibres enter largely are unknown amongst the non-malignant new-growths. It would therefore be more in strict accordance with the arrangement that has hitherto been adopted in this chapter if we postponed consideration of the malignant form of tumour which is associated with the presence of striated muscle until we come to discuss the sarcomata. It will, however, be better to deal with them here so as to keep them in close relationship with tumours composed of unstriated muscle fibres which constitute some of the commonest of the non-malignant group.

The rhabdomyosarcoma is a rare form of tumour which is practically confined to the kidney; it has, however, also been found in the ovary and testicle. Even in the case of renal tumours it is distinctly uncommon, though its characters are sufficiently noteworthy when they are seen. It is usual that a rhabdomyosarcoma is not recognised at the first glance, for the general picture of a microscopic section of the tumour is probably one of a round or a mixed cell sarcoma. In examining the specimen, however, a number of strands of fairly equal width throughout and of slightly granular, or perhaps almost homogeneous-looking, substance are seen to be scattered throughout the field. At first the impression is given that they are bands of fibrous tissue which have undergone some hyaline change, but on closer examination it is seen that they are traversed by a small amount of an indistinct transverse striation. Counter-staining with van Gieson's stain usually removes all doubt; for whereas these strands are tinted yellow by the picric acid in the stain, fibrous tissue is tinted a bright rose-red by the acid fuchsin in the mixture.

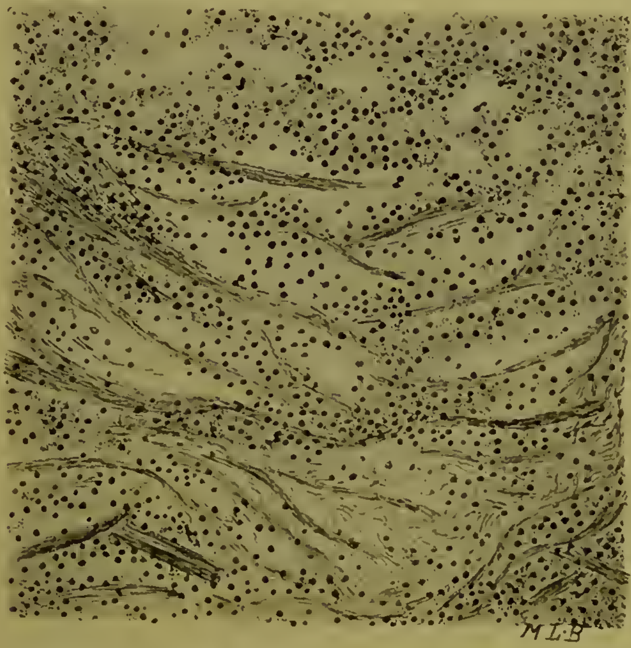

Fig. 35.—Section of Rhabdomyosarcoma. × 60.

From the kidney. The tissue is that of a round cell sarcoma with fibres of muscle traversing it in all directions. Striation is not visible with this magnification.

Rhabdomyosarcomata are chiefly found in early childhood, probably during the first year of life. It is probable that in some instances they are congenital. In any case they may form tumours of a relatively enormous size, and since, by their rapid growth, they interfere profoundly with the nutrition of the child, the weight of the tumour may be found, at the autopsy, to be nearly equal to that of the remainder of the body. It is considered that the existence of the striated muscle in the tumour is to be explained by the inclusion in the renal tissues, during early embryonic life, of a portion of the muscular plates of the abdominal wall; anatomically there is no difficulty in conceiving that such inclusion may be possible.

(*b*) **Leiomyoma.**—Tumours into the composition of which unstriated muscle fibres enter are exceedingly common, but in spite of the widespread distribution of this variety of muscle throughout the body, it is practically only in the uterus that leiomyomata are found. It is true that they have been found in the œsophageal wall, in the wall of the stomach and the intestine, in the subcutaneous tissue, as, for example in the neighbourhood of the nipple or in the scrotum, but these cases are so rare that they hardly detract from the general truth of the statement that leiomyomata only affect the uterus. An apparent exception to this statement obtains in the fact that in a fair proportion of cases of so-called hypertrophy of the prostate we have to deal with leiomyomata. Though it is by no means the case that all examples of enlargement of the middle lobe of the prostate consist of unstriated muscular tissue, it is interesting to remember in this connection that the uterus and the prostate are homologous organs. Along with the uterus we must also include the broad ligaments and the ovaries, but the latter parts are far less frequently affected.

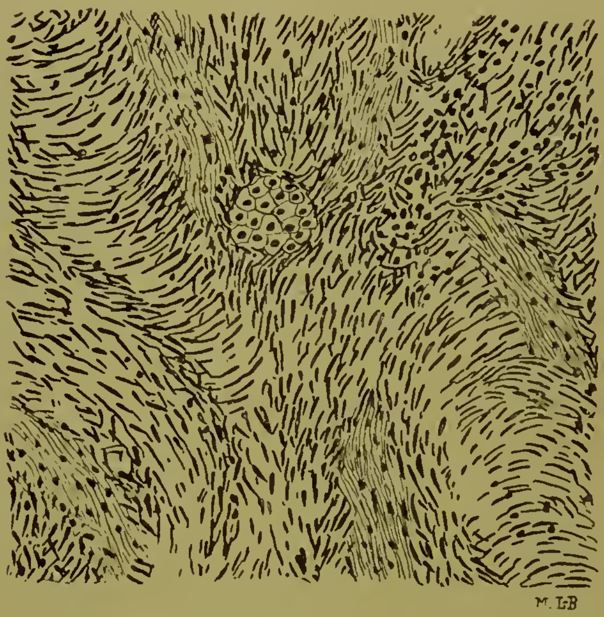

FIG. 36.—SECTION OF LEIOMYOMA. × 180.

The nuclei of the unstriped muscle fibres and the bundles of inter-muscular fibrous tissue are the chief recognisable features. In the centre is a bundle of muscle fibres cut at right angles, and throughout the figure are the round sections of nuclei that were running at right angles to the plane of the paper.

It is rare for a tumour of the uterus to be composed entirely of unstriated muscle. More commonly a certain amount of fibrous tissue enters into its composition, and fibrous tissue may predominate to so great an extent that the term 'fibroma' is more fairly applied to the tumour. In fact, it is common for these tumours of the uterus to be spoken of collectively as 'uterine fibroids.' More strictly they should be termed fibro-myomata.

The muscular tissue of a leiomyoma is identical in appearance with that which constitutes the normal wall of the uterus. It consists of a number of elongated muscle cells with a rod-shaped fairly deeply staining nucleus, and a finely granular protoplasm, in which it is sometimes possible to distinguish a faint longitudinal striation. The cells of the tumour show a marked tendency to form whorls, as is the case with the fibroma and the fibro-sarcoma. Diagnosis from a fibroma usually presents little difficulty, for the appearance of the connective-tissue fibrils and of the connective-tissue cell nuclei is pretty conclusive. But diagnosis between a leiomyoma and a fibro-sarcoma, especially if the latter be one in which the cellular elements predominate largely, is at times quite impossible.

As the result of the tendency to the formation of whorls in every direction, a section of a uterine leiomyoma, when examined microscopically, not only shows numbers of muscular fibres sweeping in all directions in the plane of the section, but also shows the cut ends of bundles of fibres which had a direction at right angles to the plane of the section. In these cut fibres the nuclei are not always severed, and consequently the portion of tissue under observation appears as if it contained fewer cells than those portions which are cut in the plane of their direction. Moreover, the effect of cutting a rod-shaped nucleus at right angles is to produce a circle, and since this circle stains in the same way as the ordinary nucleus, and, in addition, is surrounded by a thin margin of protoplasm, the effect is given of a round cell with a central round nucleus. Such appearances are of frequent occurrence in sections of the leiomyomata.

The greater the amount of fibrous tissue in a leiomyoma, the harder it is and the more likely it is to undergo change; at the same time, the less likely it is to increase rapidly in size. The principal change undergone by the leiomyomata is calcification, and it is rare to find an intensely fibrous example of the tumour in which there are not some evidences of this change. Frequently the change is so extensive that it is impossible to cut the tumour with a knife, and even a saw will divide it with difficulty.

The mucoid degeneration also occurs in myomata, but far less commonly. It usually affects the softer kinds of myoma and leads to the formation of cysts with liquid contents. In rare instances myomata take on malignancy, and then they become merged into sarcomata.

The number of blood-vessels in a fibro-myoma is usually quite small, and such as are present are principally to be found in the connective tissue which forms the capsule of the growth. This fact is important, for in the case of uterine fibro-myomata one of the chief symptoms is profuse bleeding. This hæmorrhage, however, does not come from the vessels of the tumour, but from the congested endometrium which overlies it.

(4) THE NON-MALIGNANT TUMOURS COMPOSED OF NERVOUS TISSUE

Neuroma.—The only tumour which consists of true nervous elements, if we exclude the rare form of tumour known as the ganglionic neuroglioma of which short mention has been made above, is the neuroma. Even this form of tumour is decidedly rare, most of the so-called neuromata being nothing more than fibromata which are situated upon nerves and have originated from the connective tissue forming the sheath of the nerve; they are therefore called **false neuromata.** True neuromata are practically only met with in the bulbous formations that occur at the severed extremities of nerves which have been divided in the amputation of a limb. These terminal swellings of the nerves have been rejected from the category of the tumours by some authors for the reason that they have certain relations with inflammation. But it is by no means in all cases that we find that the nerves in a stump are bulbous, at all events to such a degree as to form a tumour, and further the terminal portion of a divided nerve consists of fibrous tissue in the majority of cases, and not of a formation such as characterises the true neuroma. For these reasons, whether we regard the terminal neuromata as evidence for the mechanical irritation theory of the causation of tumours or not, we are compelled to allow that the terminal neuromata found in amputation stumps are true tumours and not merely inflammatory hyperplasias.

The neuroma consists of a tortuous mass of connective-tissue fibrils among which there ramify more or less numerous nerve fibrils derived from pre-existing axis-cylinders in the nerve above.

Sometimes these newly formed nerve fibrils can be seen to branch (fig. 170).

A variety of neuroma has been described, but is excessively rare, in which the claim of the swelling to a place among the true tumours as a neuroma is less doubtful than in the case of those modifications of nerves which have been described above. Reference is here made to the **plexiform neuroma**, a growth which is usually multiple, but affects a single definite system of nerves on the head, or the extremities, or some other part of the body. In some cases of this kind there has been found, along with a plexiform arrangement of the nerve fibres and a more or less moniliform alteration of their shape, a definite new formation of nerves. At the same time there is also a new formation of connective tissue which takes an important part in the constitution of the neuroma. The newly formed nerves in these cases are usually medullated, but plexiform neuromata containing non-medullated fibres have been described.

(5) THE NON-MALIGNANT TUMOURS COMPOSED OF GLANDULAR TISSUE

(*a*) **Adenoma.**—The adenoma is a neoplasm which may be built up of tissue that either resembles those glands of which the epithelium is columnar—e.g. the tubular glands of the intestine—or those of which the epithelium is spheroidal, e.g. the mammary gland. The general characters of the growths in these two cases also conform to the characters of the tissues which are their prototypes. For those secreting glands which are lined by a columnar epithelium form tubes, while those which are lined by a spheroidal epithelium form alveoli or acini which are filled with cells. Hence among the adenomata we meet with two varieties of growth, the **tubular** lined by a single layer of columnar epithelium, and the **alveolar** in which there are alveoli completely, or sometimes nearly, filled with cells which are fundamentally spheroidal, though the actual shape may have become distorted as the result of mutual pressure. To these two classes a third may be added which is really little more than a subdivision of the tubular variety, viz. the **papillary** adenoma. In it the connective tissue which forms the wall of the tube is thrown into the cavity of the tube and produces a papillary projection covered, of course, by a columnar epithelium like that which lines the rest of the tube. The papillary adenomata are usually definitely cystic.

In the formation of the adenoma, besides the new-formation of the epithelium which constitutes the characteristic feature of the growth, there is a new-formation of connective tissue which supports the tubules or acini and also serves to carry the nutrient blood-vessels into the growth. This connective tissue may be present in small or in large quantity, it may be highly or slightly cellular, and according to these factors the growth itself may be very firm or may be relatively soft. Thus a fibro-adenoma of the breast may be so dense that it grates when cut with the knife, and when examined by the microscope shows only the presence of a few clefts lined by a single layer of columnar epithelium, while an adenoma of the prostate may consist of little else than large irregular tubular spaces branching in all directions, with so little supporting substance between them, that it forms a tumour hardly denser than brain substance.

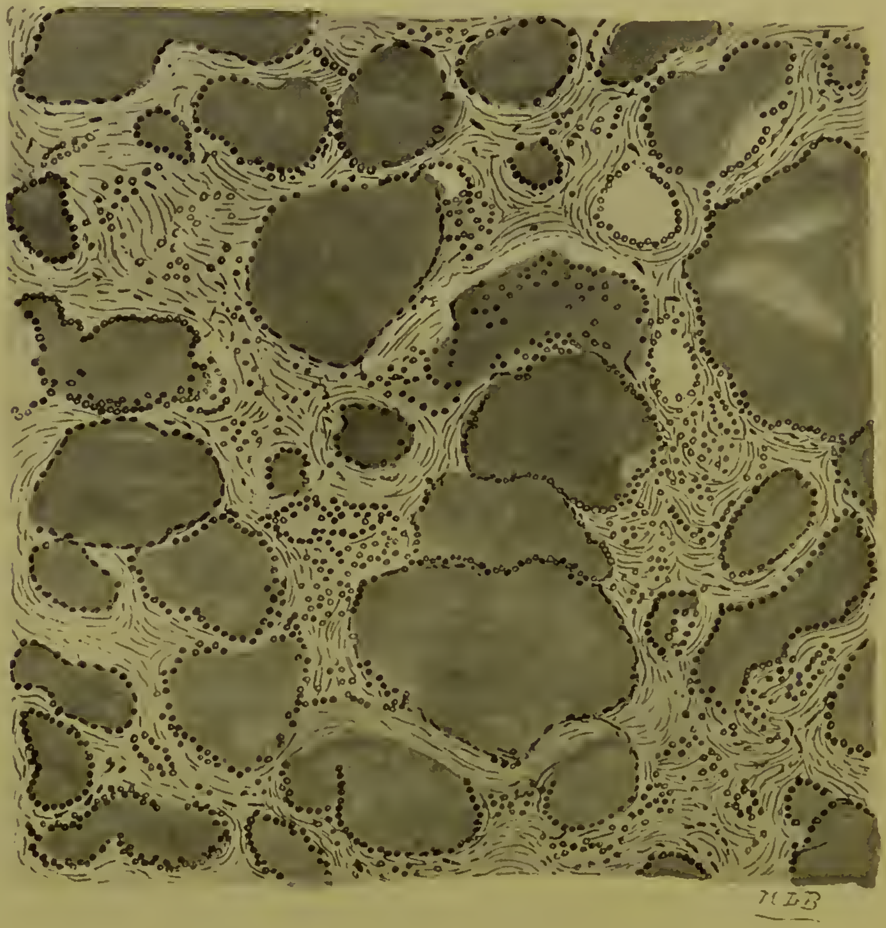

Fig. 37.—Section of Tubular Adenoma of Thyroid. × 480.

The growth consists of a number of tubes of fairly regular shape lined by a layer of flattened epithelium, filled with colloid material, and separated from one another by a small quantity of well-formed fibrous tissue.

The adenomata have a further characteristic in common with normal glands. The epithelium of an acinus of a normal gland breaks down into the secretion, or at least a secretion is the result of the activity of the epithelial cells. In the case of the adenomata some trace of this function of the epithelium is still perceptible. For in the clefts and spaces of a tubular adenoma it is almost always possible to find some material of a granular nature when hardened sections of the growth are examined by the microscope, and in many instances the substance is present in sufficient quantity to convert the tubular spaces into cysts. It is, of course, not the case that this material is in its composition identical with the normal secretion of the gland in which it is situated; but though the material in the clefts in a fibro-adenoma of the breast, for example, is not milk, it is an indication that the cells which formed it are fundamentally secreting cells. In those cases in which the normal secretion of the gland is a substance of a fatty

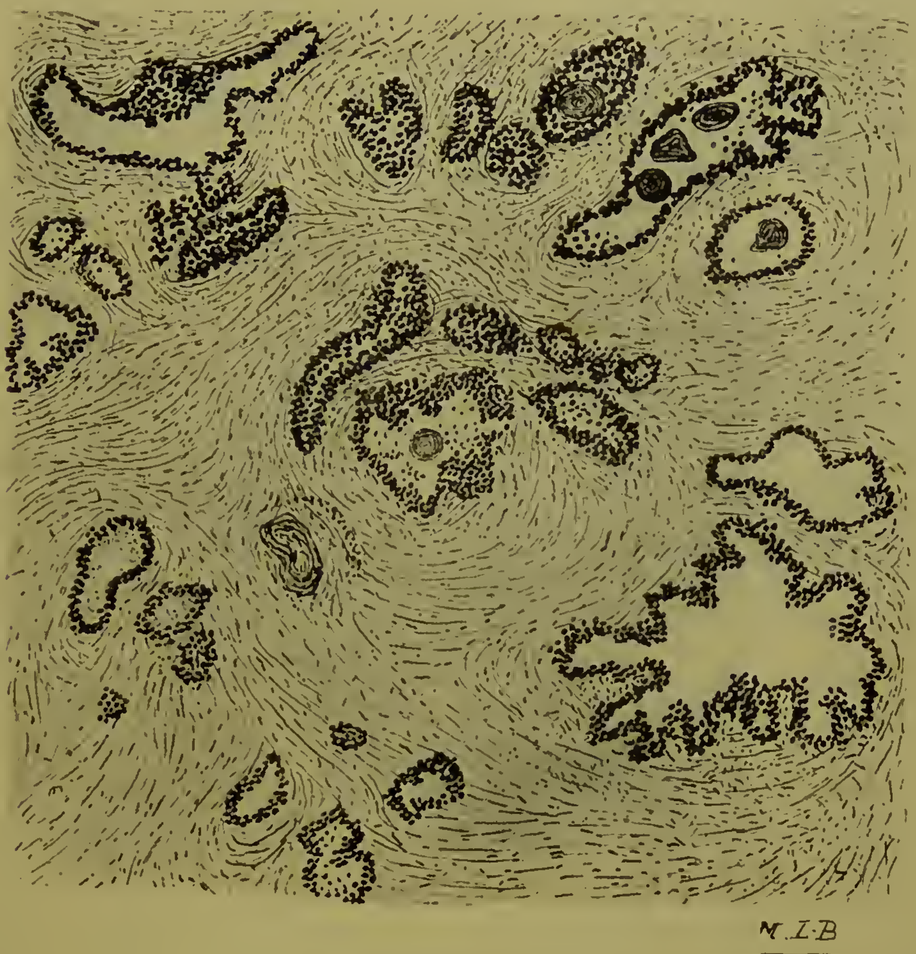

Fig. 38.—Section of Papillary Adenoma. × 420.

From the prostate. The growth consists of adult fibrous tissue, with numerous cavities lined by epithelium, into which sprout papillary processes. Four of the cavities contain corpora amylacea.

nature—e.g. sebaceous gland—the difference between the substance present in the clefts of an adenoma formed in the gland, and true sebaceous substance is less evident.

But in spite of the many points of resemblance between a true gland and an adenoma, it is usually possible to distinguish between them with ease. For the adenomata are always provided with a more or less well-defined capsule formed at the expense of the surrounding tissues; they differ in consistency from the normal surrounding gland substance, being either denser or softer, or perhaps cystic, and the character of the acini of which they are composed, as well as that of the supporting connective tissue, is different from that present in a normal gland.

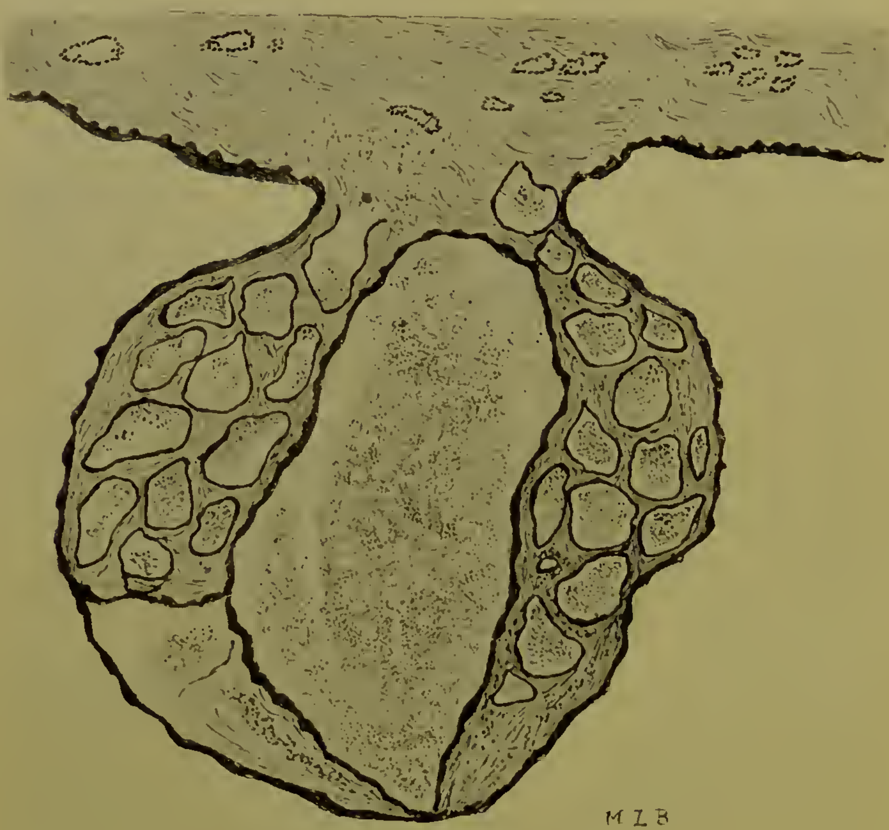

Fig. 39.—Section of Sebaceous Adenoma. × 8.
From the thigh. The tumour is covered by epidermis, and shows numerous irregular cavities of varying size containing sebaceous material.

The acini or alveoli of an adenoma are always far more irregular in size and in shape than is the case in normal gland tissue of the same type. Frequently they are branched at one extremity or both, sometimes the walls are so closely applied as the result of pressure that one only sees an irregular line of nuclei, and at other times, though the amount of fibrous tissue present in the growth is considerable, the clefts or acini are well marked and show a definite central cavity. With regard to the connective-tissue stroma, we find that when it is scanty it usually differs little in character from normal fibrous tissue in glands, though even then it is generally present in larger quantity, but when it is present in considerable amount it is usually dense, and its arrangement resembles that found in simple fibromata in that it shows a great tendency to the formation of whorls. It must be allowed, however, that in many tubular adenomata we meet with a regular and orderly arrangement of the epithelial cells which cannot be excelled in any normal tissue.

The adenomata form tumours which vary in size considerably; in the case of the breast, which is a very favourite seat for these growths, they usually lie between the sizes of a hazel-nut and a walnut, but they may be seen as large as the fist. In the prostate, which is another favourite region for their occurrence, they may be small and give rise to no symptoms, or they may cause marked enlargement of the gland and lead to serious symptoms. On occasions, they may be as large as the two fists.

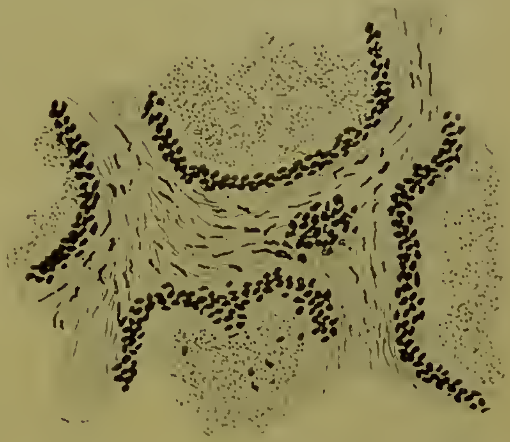

Fig. 40.—Sebaceous Adenoma. Portion of Septum between adjacent Cavities. × 420.

The septum consists of adult fibrous tissue, and the cavities are lined by a regular flattened epithelium.

In certain situations the adenomata become polypoid. This is particularly the case with adenomata of the intestine, and indeed most of the polypi of the intestine generally, and especially of the rectum, are pendulous adenomata. It is unfortunate that under the term 'polypus' so many different forms of histological structure are included.

It is hardly necessary to note that the adenomata are, of course, of either epiblastic or hypoblastic origin so far as the strictly epithelial elements are concerned, but it is well to remember that the mesoblast enters into the composition of all complex glands in virtue of their supporting connective tissue and the blood-vessels which it carries. This fact becomes of considerable importance when we are dealing with the malignant neoplasms of glands. (See also figs. 152 and 153.)

(*b*) **Lymphoma, lymphadenoma.**—These two terms are often used interchangeably, but often the term lymphoma is used to signify any tumour consisting of tissue similar to that of lymphatic glands, and is qualified by the names 'non-malignant' and 'malignant' according to circumstances.

A gland which is affected with lymphoma or lymphadenoma consists of a delicate connective-tissue stroma in the meshwork of which are crowded numbers of cells. These cells are in appearance lymphocytes; that is to say, they are small round cells with a small round nucleus which practically occupies the whole of the cell and stains deeply with basic dyes; they bear no granules in their protoplasm, and the amount of that protoplasm is small. The appearance of the lymphadenomatous gland, therefore, does not greatly differ from the appearance of a lymphatic gland affected by simple inflammation, so that it is practically impossible for one to determine from the mere examination of a microscopic section, whether the gland has been the seat of simple inflammation or is the seat of a true tumour. That it is not normal we may perhaps be able to say with certainty, but we cannot go further than this.

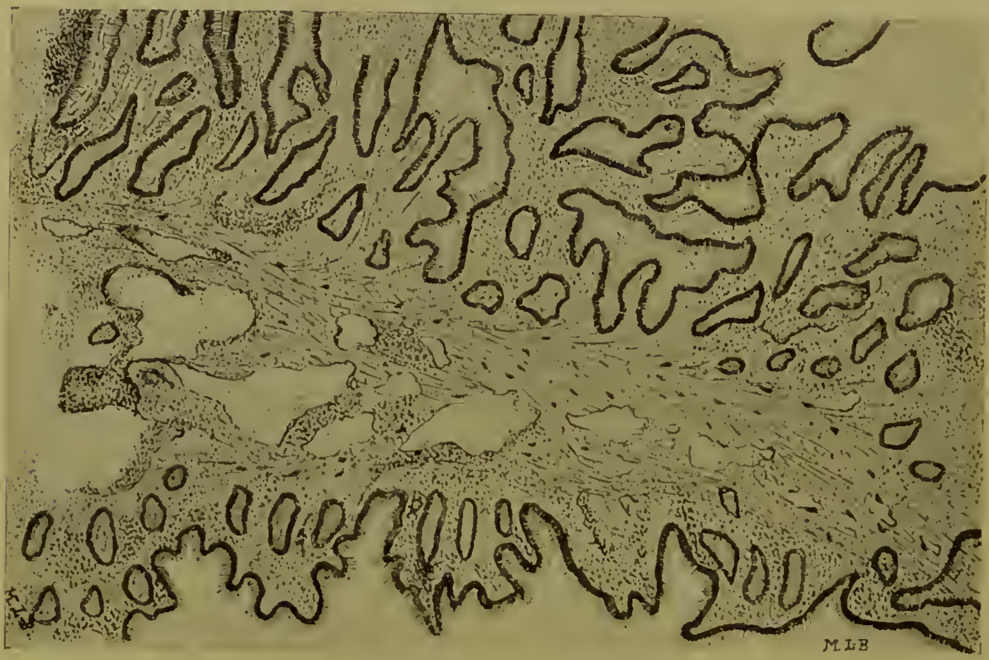

FIG. 41.—PORTION OF 'INTESTINAL POLYPUS' (PENDULOUS TUBULAR ADENOMA). × 40.

From right to left in the figure runs a band of adult fibrous tissue, which carries the blood-vessels, and is continuous with the sub-mucous connective tissue. The irregular tubular portions above and below are covered by columnar epithelium, and were continuous with the intestinal mucous membrane.

But though the histological appearances of the affected glands are so difficult to recognise, it is different with the macroscopic picture of the disease itself, in which that enlargement is so commonly seen. To this, and to the changes met with in the blood, reference will be made later.

Bearing in mind the impossibility of making a histological differentiation between the condition of the lymphatic glands in the disease with which we have been concerned in the preceding paragraphs, and the modification of glands which occurs when they are the subject of a chronic irritation, some authors have maintained that lymphadenoma is in reality an inflammatory condition, and not one of true tumour formation at all. Indeed the matter has been carried so far that numerous attempts have been made to cultivate micro-organisms from the affected glands. In several cases such micro-organisms have been obtained, but at present it is not held by the majority of pathologists that a convincing case has been made out for the bacterial view. Some authors believe that lymphadenoma is nothing more than tuberculosis affecting lymphatic glands.

Although the lymphomatous glands constitute what is strictly a non-malignant formation, in the sense that the glands do not invade surrounding tissues and do not form secondary growths, neither do they recur locally after removal, the actual course of the disease is a progressive one towards death. For the number of the glands affected is so great, the size to which they attain is so considerable, and the number of situations at which enlargement may take place so indefinite, that in some region or other the masses of glands come to exert mechanical pressure upon a vital structure. Frequently the trachea or some other portion of the respiratory tract is the especial region by way of which death is produced. It is clear that when the glands are intra-thoracic their increase in size will produce a relatively greater effect, and will, proportionately, be more dangerous.

SECTION IX

THE NEW-GROWTHS OR NEOPLASMS—continued

THE MALIGNANT TUMOURS

A.—The Sarcomata

It has already been said that the malignant tumours are divided into two classes according as they are built up of cells which have their prototype in cells of the connective-tissue group, or as they are built up of tissue into the composition of which epithelial cells enter. These two classes constitute the **sarcomata** and the **carcinomata** respectively. Consideration of the carcinomata will contribute the subject matter for the next chapter.

Speaking generally, the sarcomata are relatively simple tumours so far as their histological characters are concerned. They consist of cells which may have different shapes, may belong to different members of the connective-tissue group, may originate in different parts, may grow with more rapidity in one case than in another, but histologically they consist of cells and the substances that those cells produce immediately around them. Blood-vessels they have none in the strict sense of the word, for the channels in which the blood for their nutriment is contained, though they may be of considerable size and very numerous, are little more than clefts or spaces between the cells. So, too, the sarcomata are devoid of lymphatics and of nerves.

The sarcomata are distinguished in part by the characters of their cells and in part by the nature of those cells. Hence we meet with round, spindle, oat, mixed, and giant cell sarcomata on the one hand, and osteo-, chondro-, rhabdomyo-, glio-sarcomata on the other. Of these two groups, that which consists of members which are composed of cells distinguished only by their shape, is the simpler from the histological point of view, though it is not infrequently the more complicated from the clinical point of view. We shall commence with this group.

(*a*) **Round cell sarcoma.**—It is usual to divide this class into those in which the cells are large and those in which the cells are small. At times it is difficult to decide into which class a given specimen shall be placed, but as a rule it is relatively easy. The large round cell sarcoma consists of cells which have a large round nucleus set in a large amount of protoplasm, so that the actual size of the cells of which the tumour is composed are larger than any cells met with in the body, with the exception of giant cells and the large ganglionic cells of the brain and cord. The nuclei stain deeply with basic dyes, and it is often easy to distinguish the chromatin network. Often, too, evidences of cell division may be seen either in the presence of two nuclei in one cell or in that of karyokinetic figures in the nucleus itself. In any case there is always evidence that the tumour from which the cells were taken was growing rapidly.

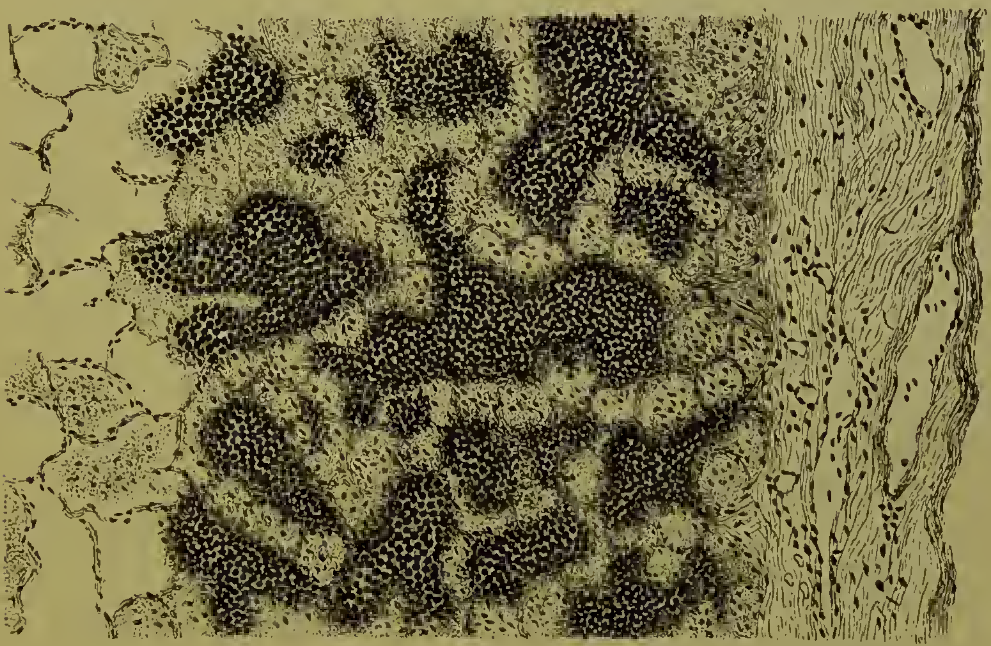

Fig. 42.—Large Round Cell Sarcoma invading Lung. × 60.

On the right is the thickened visceral pleura, on the left lung tissue which is partly emphysematous, partly broncho-pneumonic. The middle portion of the figure shows masses of nuclei of sarcoma cells (dark), which have invaded the lung, breaking down the alveolar walls, and intervening masses (light) of lung tissue that is compressed, airless, and ready to be invaded by the extending masses of sarcoma tissue.

Strictly speaking, between the individual cells composing a round cell sarcoma we should find some substance (corresponding with the fibres of fibrous tissue) which has been produced by the cells at the expense of their own protoplasm. Though, as we shall see, it is often not difficult to determine the presence of such a substance in the case of the sarcomata composed of spindle cells, it is by no means easy to satisfy oneself of the existence of such an inter-cellular material in the case of the round cell sarcomata. The reason of this is evident. For the round cell sarcoma represents a connective-tissue cell in a less differentiated condition than the spindle cell—a condition, that is, more embryonic in its development. And since in the early days of the embryo we find that the mesoblast consists of cells alone, and that it is only a little later that these cells give evidence that one of their principal functions is to form an inter-cellular substance, so when we have to deal with a sarcoma composed of round cells we find that the existence of an inter-cellular substance is more a matter of faith than one of sight. That there may be definite septa of connective tissue breaking up the entire growth into segments of different sizes there is no doubt, but it is not of the major partitions that we are speaking, but of those partitions which, by our fundamental conceptions of the nature of a connective-tissue cell, we expect to see between the individual cells.

Nor are the characteristic shapes of the cells easy to make out if a section of the tumour alone is examined. The shape and size of the nuclei are to be determined with ease, but unless we take special means the shape of the cell itself is never seen. For this purpose it is necessary to examine scrapings of the surface of the tumour, and the material obtained by scraping should first be examined without staining in a small quantity of ·75 per cent. salt solution, and subsequently a trace of some such dye as methylene blue in dilute watery solution should be run in at one side of the cover-slip. If these precautions be taken, it will be possible to recognise many features of the cells that are completely lost if only sections stained by the ordinary methods are examined.

The large round cell sarcoma is not a very common form in which we meet with sarcomata, but the small round cell variety is one of the commonest. In it the cells have an appearance exactly similar to those which have been described above as characterising the large cell variety, only the size of the cells themselves and that of their nuclei is smaller. In spite of this fact, however, the actual size of the cells is greater than that of most normal cells having a similar appearance. For example, it is common for the small round sarcoma cell to be distinctly larger than a lymphocyte, the cell to which it has the greatest amount of resemblance. This excess of size is chiefly due to the greater amount of protoplasm in the sarcoma cell; for the nuclei in the two cases are very similar in size as well as in shape and staining reactions.

(*b*) **Spindle cell sarcoma.**—The spindle cell sarcomata are composed either of large or of small spindle cells, and with this difference one description will serve for both varieties. The fundamental form of the cells in this kind of sarcoma is that of a spindle. That is to say, the cell is elongated and tapers at either extremity to a point. Not infrequently, however, the extremities bifurcate. This bifurcation may take place at one or at both ends, and the branches may be quite small or they may equal the body of the cell in length. At the same time the nuclei of the cells have a characteristic shape, being elongated, somewhat rod-like, with slightly tapering ends. The cell protoplasm stains faintly, but relatively to the protoplasm of other cells deeply ; the nuclei commonly stain somewhat lightly and the chromatin network is usually well shown. The nuclei have a great resemblance to the nuclei of unstriped muscle fibres, and in a microscopic section it may be impossible to distinguish between the two varieties of cell.

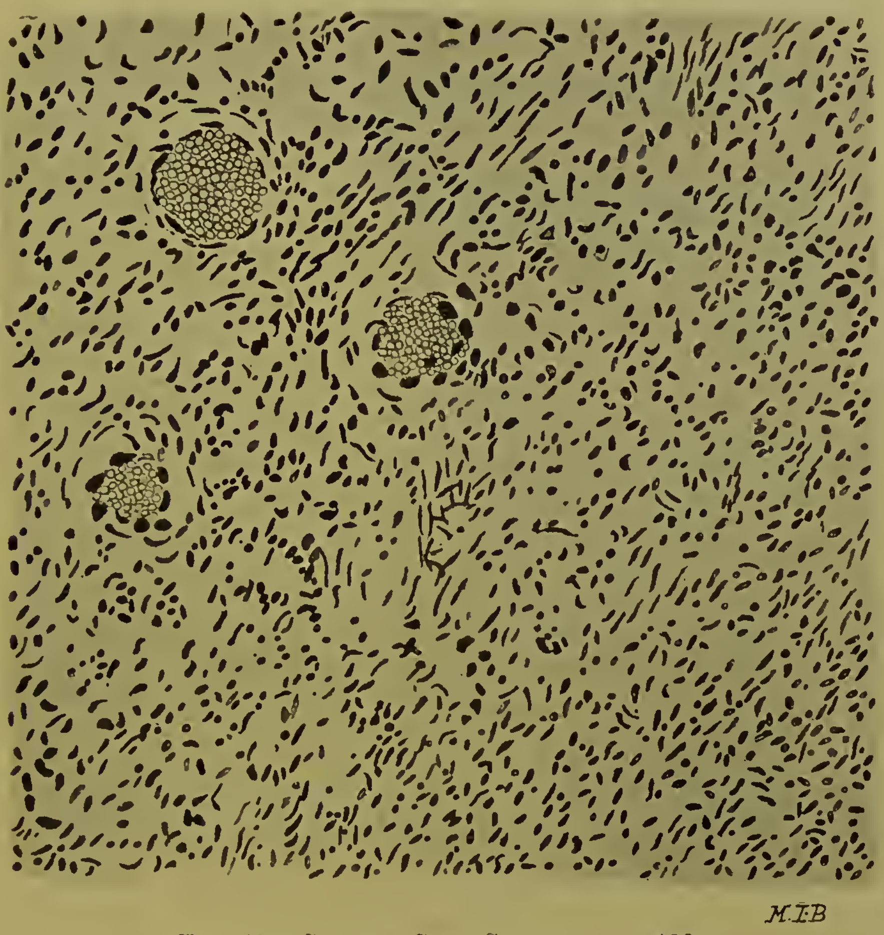

Fig. 43.—Spindle Cell Sarcoma. × 480.

In a section only the nuclei of the cells are discernible. These are fusiform, or on section round or oval. Compare with fig. 36. The indefinite wall of the blood-vessels in sarcoma is well shown.

Evidences of karyokinesis, though seen, are not so commonly met with as in the case of the round cell sarcomata.

The general appearance of a spindle cell sarcoma in microscopic section is very similar to that characterising a simple fibroma, owing to the marked tendency there is for the formation of whorls. It follows that there is at times a great difficulty in deciding whether the section has been taken from a specimen of a fibroma or from a spindle cell sarcoma, especially when the fibroma is one that has grown rapidly or the sarcoma is one which has grown slowly. Under these circumstances it is quite impossible to give an opinion from consideration of the microscopical appearances alone. The same is true in the case of any variety of newly formed fibrous tissue, so that it may also be impossible to decide whether a given piece of tissue has come from a spindle cell sarcoma or from a focus of chronic inflammation.

(*c*) **Oat cell sarcoma.**—This variety of sarcoma is not very common; it is really a special variety of the spindle cell sarcoma. The cells of which it is composed are elongated, but not to so great an extent as the cells of the spindle sarcoma, neither do they possess extremities which taper so definitely to a point. On the contrary, the ends of the cells are somewhat rounded. A sarcoma composed of this variety of cell has a very regular aspect in microscopic section, for the cells show a great tendency to be of uniform size throughout the tumour. Otherwise there are no differences between the cells and those of a small spindle cell sarcoma which call for notice.

(*d*) **Mixed cell sarcoma.**—The mixed cell sarcoma is a very common variety. In it one meets with large and small round cells mixed indiscriminately with large and small spindle cells. Sometimes a given portion of the tumour consists of one variety to the practical exclusion of the others, but at a short distance a portion may be seen which consists almost entirely of another variety of cell. In the class of mixed cell sarcomata that variety of sarcoma which is characterised by the presence of giant cells is not included, though undoubtedly, from a merely anatomical point of view, it belongs to the class of mixed cell sarcomata in the highest degree. It is erected into a class of itself, and rightly so; for, as we shall see when considering the relative degrees of malignancy of the different varieties of sarcoma, the variety in which giant cells are present differs markedly from the members of the class constituting the mixed cell sarcomata.

(*e*) **Giant cell sarcoma (myeloid sarcoma, myeloma).**—The variety of sarcoma in which giant cells are present consists of a number of other kinds of cell besides the giant cell itself. In fact, it is always the case that cells of round or of spindle shape are far more numerous than the giant cells, although these latter are in some instances present in considerable numbers.

Concerning the other cells in a myeloid sarcoma it is unnecessary to speak, for their characteristics are in all respects similar to those of the round and spindle cells that have already been described. But a few words may be said in reference to the giant cells themselves. These cells may be large or small, they may have many nuclei or few, but it is far commoner for the cells to be of small size and for the nuclei to be few. In any case the nuclei show no tendency to be arranged in a definite manner as is in some degree the case in tuberculosis, but on the contrary their arrangement is quite indefinite. In many instances the giant cells, and especially their nuclei, are indistinct from the fact that they have undergone some degenerative change. This is more particularly the case when the section under examination has been taken from a central portion of the tumour. It is then only from other considerations that we can come to the conclusion that the homogeneous masses in question are really degenerated giant cells.

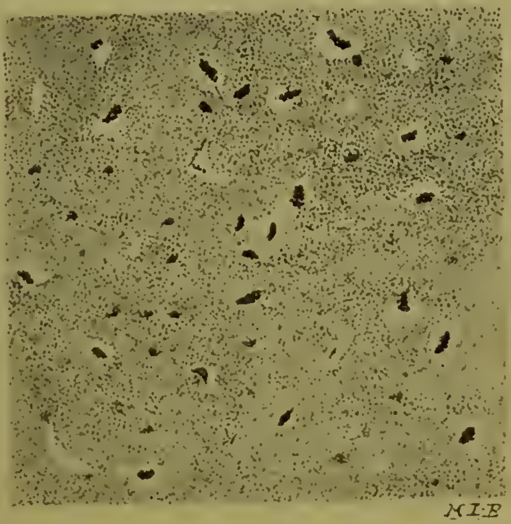

Fig. 44.—Section of Myeloid Sarcoma. × 60.

From the lower jaw. The giant cells have shrunk in the process of hardening, and seem to be in clear spaces. The bulk of the tumour consisted of mixed round and spindle cells.

It is clear that the myeloid sarcoma consists of elements similar to those met with in ordinary granulation tissue, and this is even more obviously the case than with the other forms of sarcoma. It might be expected, therefore, that the difficulty in deciding whether a given mass of tissue is myeloid sarcoma or granulation tissue should be more than ordinarily difficult. As a matter of fact, this is not the case, partly because the giant cells present in a myeloid sarcoma are usually far more numerous than in granulation tissue, but principally because the myeloid sarcoma forms a special variety of tumour, affects special tissue (bone), and even then is rarely met with except in a few situations. It must be conceded, however, that some authors refuse to the myeloid sarcoma a place among the sarcomata altogether, and, for this reason, term the new formations **myelomata.** They base their contention principally upon the belief that these forms of growth are not accompanied by the presence of secondary deposits. It is undoubtedly true that secondary deposits of myeloid sarcoma are extremely rare, but it is incorrect to say that they are never formed. The other portion of the contention which is bound up in the use of the term 'myeloma' is that the growths are really varieties of a chronic inflammation. It does not stand or fall with the question whether the growths are sarcomatous or not, for it is well known that secondary deposits are often present in cases of inflammation (e.g. tuberculosis), and there are many pathologists who are prepared to admit the possibility that the relationship between the whole group of sarcomata and inflammation is a more intimate one than that of mere histological resemblance.

(*f*) **Melanotic sarcoma.**—The melanotic sarcoma is characterised by the fact that the cells, or certain of them, possess the function of forming pigment (Plate II, c). The constituent cells of the tumours are either round or spindle in shape, and giant cells are never present. The pigment is always present in the cell protoplasm and is formed thereby. Nor is it ever found in an extra-cellular position in a tumour, though an apparent exception to this statement occurs (1) when the amount of pigment is so great that the body of the cell is completely obscured, and (2) when the cell itself has degenerated from some cause or other. The pigment varies considerably in colour even in the same tumour, and at parts no great distance from one another. It varies from an extremely pale yellow to an intense black. This is even more striking in the case of secondary deposits of the growth. In the liver, for example, we may find nodules of inky blackness side by side with nodules that are completely colourless. In this instance it does not necessarily follow that the difference in the colour of the nodules is due to a difference in the colour of the pigment alone or at all, for not all the cells of a melanotic sarcoma produce pigment, so that it is quite likely that the absence of colour in a nodule is due to the entire absence of pigment. The intensity of the pigmentation in the secondary deposits is quite independent of the degree of pigmentation in the primary tumour.

The melanotic sarcomata are formed in situations in which it is normal for pigment to be formed. Thus, their primary seat is either the skin or the choroid. An apparent contradiction of this statement is presented by the rare occurrence of melanotic sarcoma of the cerebral membranes, an example of which is recorded in the Transactions of the Pathological Society of London for 1899. This particular situation of a melanotic sarcoma is full of interest, for it was in the case referred to associated with a sarcoma of the pineal body. This body is homologous with an eye, and although it does not contain pigment in man, pigment is normally present in the pineal body of the Lacertilia. Hence the apparent contradiction is in reality a strong confirmation of the statement that the melanotic sarcomata only originate in situations in which pigment is normally formed. In the case of the skin, melanotic sarcomata are especially liable to originate in pigmented congenital moles and warts.

Though the pigment in melanotic sarcomata is intra-cellular, it is sometimes met with in a state of solution or even in a state of suspension in the urine, leading then to the condition known as melanuria. This condition generally occurs when some part of the urinary tract is the seat of secondary deposits of growth, and the pigment finds its way into the urine as the result of the degeneration and disintegration of some portion of the tumour. But in other cases the urinary tract is not affected, and then we can only conclude that the pigment has been carried to the kidneys by way of the blood stream, having been taken up at some other point at which destruction of the tumour has been going on.

The pigment itself has received the name of **melanin.** It does not contain iron, but does contain sulphur.

The melanotic sarcomata show some tendency to transmission by inheritance. The late Professor Kanthack mentioned to the author that he had known this form of sarcoma to occur in a grandmother, mother, and daughter.

Sufficient reference has already been made to the chloroma (p. 26); it is only necessary here to add that it is a round-cell sarcoma, and that it especially affects the periosteum of the skull. It is excessively rare.

(*g*) **Psammoma.**—This is a variety of sarcoma that is met with in the membranes of the nervous system, and particularly in the choroid plexus and the pineal body. It is usually a round-cell sarcoma in which the cells are few in number and have most of them undergone a myxomatous degeneration. But the characteristic feature of the growth is that it shows the presence of a smaller or greater number of calcareous granules ('brain-sand'). These granules are not arranged in so indefinite a manner as in the case of a sarcoma that undergoes calcareous degeneration, but the grains themselves appear to consist of concentric rings somewhat like those which are characteristic of the corpora amylacea of the prostate. The granules may be recognised with the naked eye as white particles which grate when scraped with a knife. The psammomata do not form large tumours, and it is not infrequent to find that one is present on the fringe of each of the prolongations of the choroid plexus that pass into the lateral ventricles. As a result of the degenerative processes that accompany the formation of these growths, they are often cystic. The psammomata are rather of pathological interest than of clinical importance.

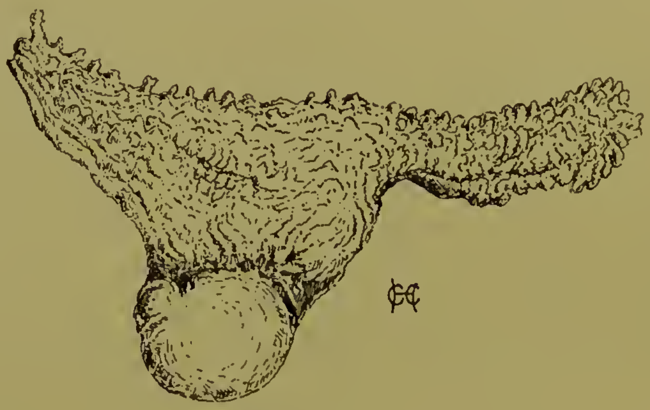

FIG. 45.—PSAMMOMA. NATURAL SIZE.

From the choroid plexus of the brain. The growth was of gelatinous consistency, with occasional cretaceous masses of 'brain-sand.'

(*h*) **Alveolar sarcoma.**—In the descriptions of the preceding forms of sarcoma we have been chiefly concerned with the shapes of the cells of which the tumour is composed. In the case of the alveolar sarcoma we have to consider the arrangement of masses of cells.

It is a characteristic of the sarcomata that there is a certain amount of inter-cellular substance in every part of the tumour, although that substance may be very difficult to make out when the tumour is highly cellular. In most cases the inter-cellular substance is fairly evenly distributed throughout the tumour, so that a microscopic section has a more or less regular appearance. But sometimes the inter-cellular material is not evenly distributed. When this is the case, and when the inter-cellular substance is fibrous, the tumour is intersected by bands of connective tissue which interlace in all directions. These trabeculæ of the tumour are very obvious, and if the inter-cellular substance in the portions of tumour between the trabeculæ is scanty and delicate, the appearance given is that of a tissue consisting of masses of cells contained in alveoli and not separated from one another, but, on the contrary, in absolute contact.

It is in the sense conveyed in the preceding paragraph that a considerable number of the alveolar sarcomata are to be interpreted, but a class of tumours which was formerly included among the carcinomata was at one time included among the alveolar sarcomata. Reference is here made to that group which is now spoken of as the **endotheliomata**, concerning which more will have to be said later. These endotheliomata may with even more justice be included among the alveolar sarcomata than those forms in which there is an irregular distribution of the connective tissue traversing the tumour. But since they have been erected into a special group, the class of alveolar sarcomata falls to the ground unless we employ it to include tumours such as have been described in

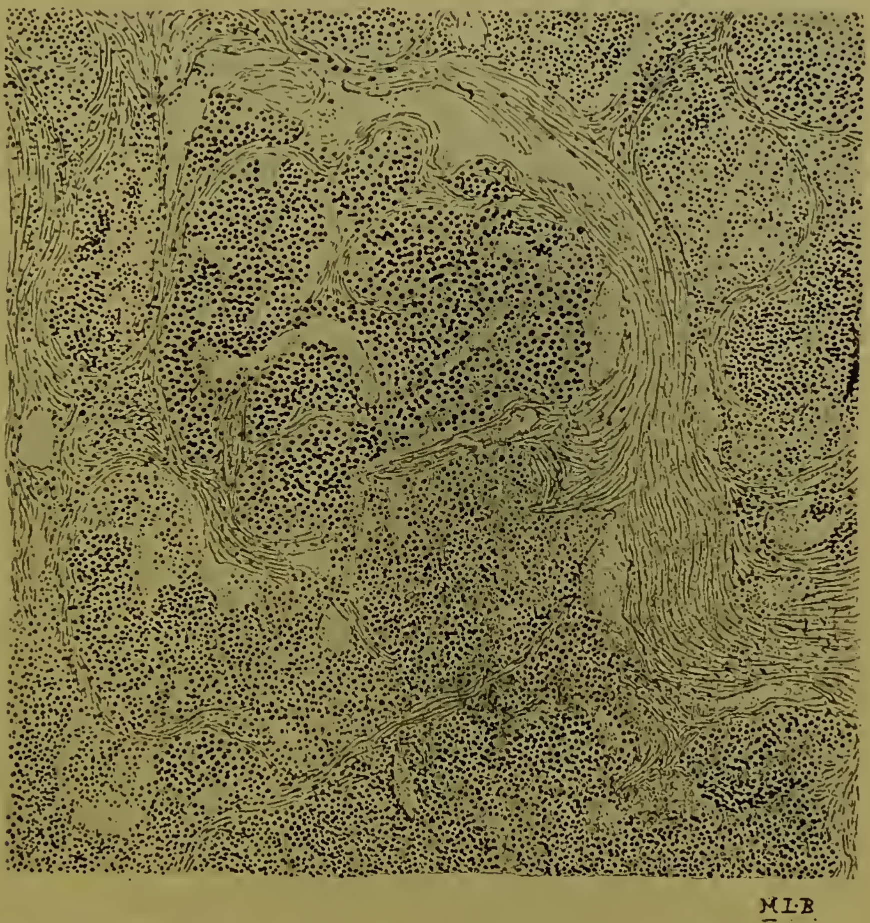

FIG. 46.—SECTION OF ALVEOLAR SARCOMA. × 60.
A round-cell sarcoma divided up by irregular fibrous trabeculæ.

the first paragraph. This is not inconvenient, for the tumours in question have anatomical characters which justify us in separating them from the rest of the sarcomata in some degree.

Having considered the characters of the sarcomata so far as the cells of which they are composed are concerned, we must now consider some of the more important varieties of sarcoma so far as their more complex structure comes into the question. Among these the most important are certain forms in which the intercellular substance has a more definite form than mere soft substance or even than fibrous tissue itself. In them we find cartilage (chondro-sarcoma), calcifying material (calcifying sarcoma), or bone (ossifying sarcoma, osteo-sarcoma). These three varieties have so much in common that they may be considered together.

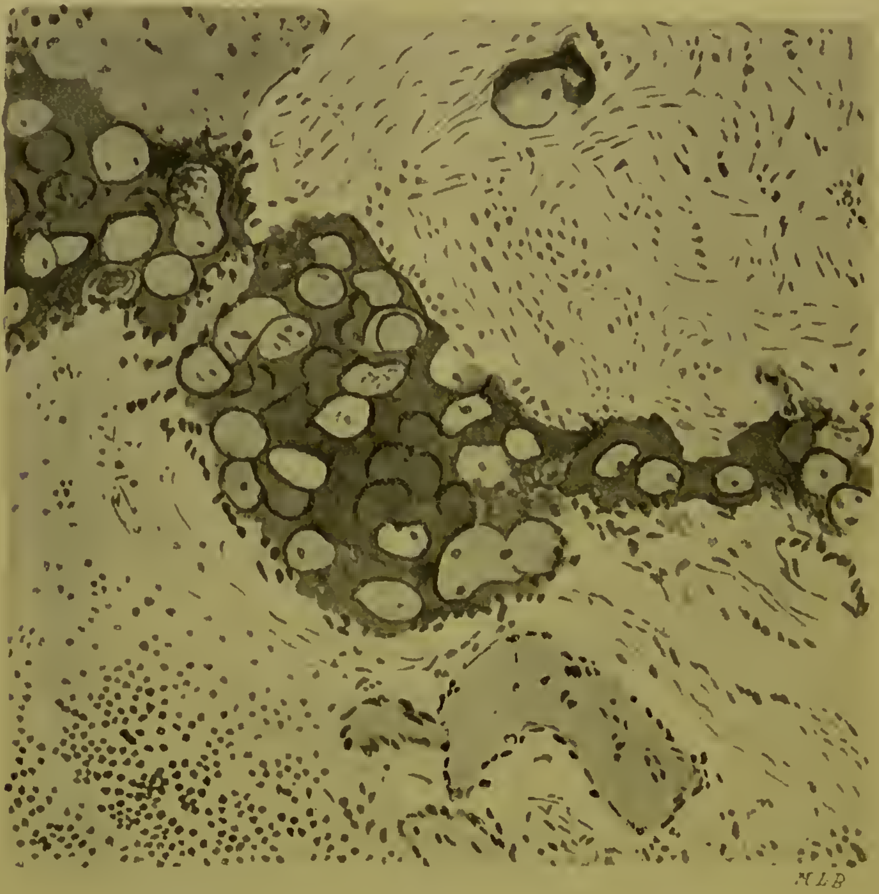

Fig. 47.—Section of Chondro-sarcoma. × 420.

The tumour consists of irregular masses of hyaline cartilage (dark), with or without large spaces containing cartilage cells. The adjacent tissue is sarcomatous, the cells being round (below) or mixed (above). The nuclei alone of the cells are visible. At the margin of the masses of cartilage is a fairly regular layer of large cells with large oval nuclei.

Of the three varieties the **chondro-sarcoma** is less common than either of the two others in a pure form. Mixed up with the calcifying or the ossifying forms it is not very rare. It originates from some part which is cartilaginous during extra-uterine life, or more frequently from some part which was cartilaginous at an earlier period. Hence it is chiefly found in connection with bone, and then it is probable that it has risen in an 'embryonic remnant' of that cartilage which was the precursor of the fully formed bone.

It is also met with in tumours of the parotid gland, the testis and ovary, and sometimes in those of the kidney. In these situations a plausible explanation is afforded by the embryological history of the part, the cartilage being, in the case of parotid tumours, derived from a portion of a branchial arch, and in the case of the other organs mentioned derived from portions of the cartilaginous precursors of the vertebral column. In most cases the chondro-sarcomata form numerous secondary growths, and, following the general rule as to the secondary growths among the malignant tumours, the metastases also consist in part of cartilage, whether the tissue in which those metastases are formed normally contains cartilage or not.

The **calcifying sarcomata** are really only examples of the occurrence of calcareous change in the inter-cellular substance of a sarcoma, though something more than this is usually implied in their existence. For the calcifying sarcomata almost always arise in connection with the periosteum, that is, in connection with a tissue normally occupied with the deposition of calcium salts in inter-cellular substance formed by its cells. The calcareous material, therefore, is not disseminated without arrangement through the tumour, but, on the contrary, forms spicules which extend into it from the point at which it arises from the periosteum. Following the lines of growth of the tumour, these spicules of calcareous material not only extend outwards from the periosteum, but also pass inwards into the lumen of the bone or into the cancellous tissue of either end of it; the original bone itself having largely disappeared, as the result of the pressure atrophy induced by growth of the soft parts of the tumour. Hence if any bone which has been the subject of such a tumour is macerated, it is found to be surrounded on the outside by a mass of stalactitic projections of calcareous material, while the original tissue of the bone itself seems thicker than normal because of its replacement by an excessive amount of a calcareous substance which has many of the macroscopic features of bone. Histological examination, however, proves that the tissue in question is not bone, for no Haversian canals are present even in a rudimentary form; it is only a fibrous tissue which has been the seat of calcareous deposit. Owing to its resemblance to that variety of sarcoma in which true bone is formed, the calcifying sarcoma has received the name of **osteoid sarcoma** at the hands of some authors, but it is better to use the expression **calcifying** in order to lessen the chances of confusion.

In the **osteo-sarcoma** true bone is formed—that is to say, the inter-cellular substance consists of a calcareous material which is arranged more or less concentrically around blood-vessels, and which is formed by the agency of cells having close analogies with normal osteoblasts. The tumour, therefore, contains the elements of Haversian canals, although it must be confessed that it is more accurate to speak of irregular blood spaces than of Haversian canals. The ossifying sarcoma or osteo-sarcoma forms bone without the intervention of cartilage, whether the bone from which it originates was laid down in cartilage or in membrane. The chondro-sarcoma, contrary to what one might perhaps

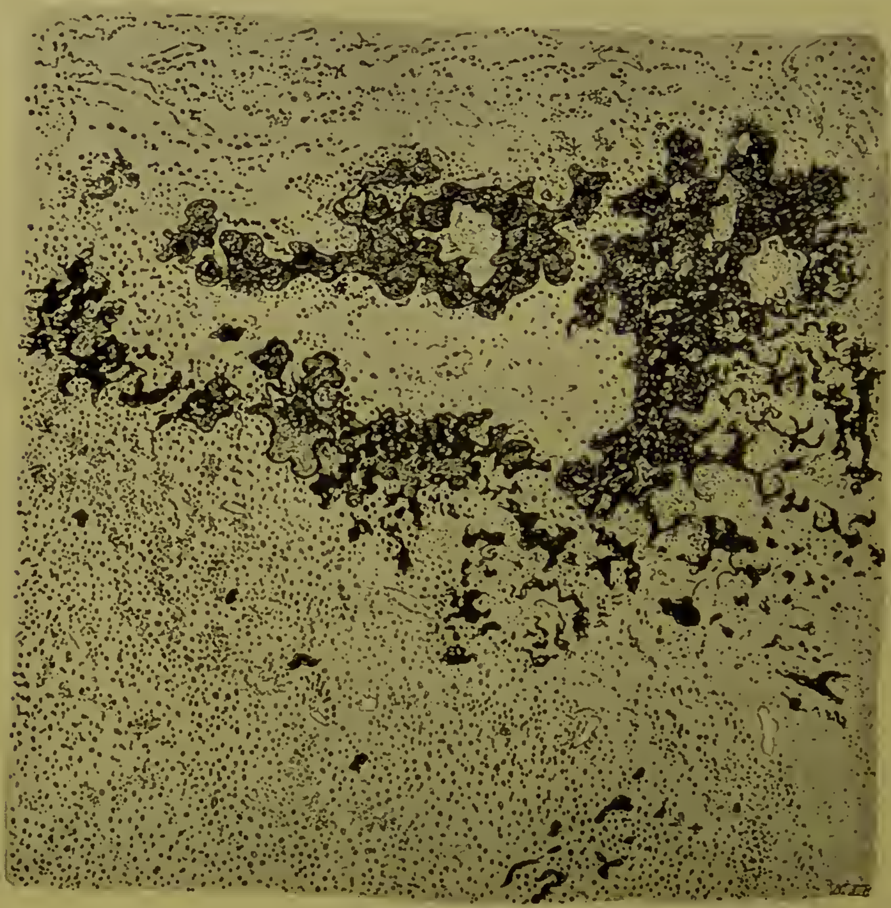

FIG. 48.—SECTION OF OSTEO-SARCOMA. × 60.

The dark masses consist of irregularly formed bone. The surrounding tissue is sarcomatous, principally of the round-cell, but partly of the mixed-cell variety.

expect, does not lead to the formation of an ossifying, but to the formation of a calcifying, sarcoma, although it is not infrequently accompanied by small portions of bone in the tumours which it constitutes.

When other more complex tissues become sarcomatous, they generally lose entirely their characteristic features and become converted into one or other of the simple forms of sarcoma. Thus when the neuroma becomes sarcomatous the tumour maintains its connection with the nerve, it is true, but otherwise there is no evidence that nerve tissue has at any time entered into its composition. For it exists only as a spindle-cell sarcoma which follows the ordinary rules of growth and histological structure of such a growth. The same is true in the case of the leiomyoma, except that at some point or other of the entire tumour it will probably be possible to distinguish a portion of the original growth which has not undergone the malignant change; here, too, the malignant growth will be a sarcoma, and in all probability one of the spindle-cell variety. To the rhabdomyo-sarcoma we have already referred; in it there is to be recognised a certain amount of striated muscle fibre, though the bulk of the tumour is made up of round sarcoma cells. The glioma, too, usually maintains a portion of its particular features, so that a glio-sarcoma is a form of growth that can be distinguished readily. The same is true of the myxo-sarcoma.

The **lympho-sarcoma** is a form of tumour which has certain characteristics, though it must be conceded that they are not always easy to make out, and that there is not that unanimity among pathologists as to the histological characters which shall be taken to distinguish the variety that could be wished. By some authors the term is held to be synonymous with lymphadenoma, but the clinical features of that disease, which we shall describe later under the name of lymphadenoma (Hodgkin's disease) are so different from those found along with lympho-sarcoma that it is desirable to differentiate between the two. Added to this is the fact that the histological characters of a lymphatic gland the seat of lymphadenomatous change are different from those of one which is the seat of lympho-sarcoma. These differences are as follows. First, in lymphadenoma the glands, though enlarged, show no tendency to become fused into one mass as they do in the case of lympho-sarcoma, but, on the contrary, remain discrete to the end. Second, in lymphadenoma there is a tendency for all glands of the body, or, speaking more exactly, for all the lymphoid tissue of the body, to share in the general overgrowth, so that the condition has more resemblance to a generalised hyperplasia than to true tumour formation; but in lympho-sarcoma the change more probably affects one particular system of glands, e.g. those in the neck or in the posterior mediastinum. Third, in lymphadenoma there is usually some increase in size of the spleen, and at times this increase is very considerable; in lympho-sarcoma, on the other hand, the spleen need not be, and frequently is not, affected at all. Fourth, the histological features of a lymphadenomatous gland are such that it is impossible to distinguish a section taken from it from a section of a gland the seat of simple adenitis; indeed it is often difficult to distinguish it from a section of a normal gland, whereas the lympho-sarcomatous tissue has certain features of its own.

It may be possible to select for microscopical examination a portion of a mass of lympho-sarcoma which still retains the anatomical outline of a lymphatic gland, but not infrequently this is impossible owing to the fact that all boundaries have been lost because of the extension of the growth from one gland to its neighbours and to surrounding tissue that was not originally lymphoid. The actual structure of the growth, too, is totally unlike that of a normal lymphatic gland, if we except the point that the cells which make up the tumour are small round cells with a relatively large and deeply staining nucleus. That is to say, the bulk of the cells are of a kind which it is impossible with our present means to distinguish from lymphocytes, but the stroma in which they are placed, and the position which they hold relative to that stroma, are different. For little stroma though there is in a normal lymphatic gland, there is considerably less in lympho-sarcomatous tissue, neither is there any appearance of the normal lymph channels. In a lymphadenomatous gland lymph channels have disappeared owing to the number of cells with which they are crowded, it is true, but in lympho-sarcoma they have been abolished. Hence a microscopic section of lympho-sarcoma shows a mass which consists almost entirely of small round cells with darkly staining nuclei. These cells do not appear to be separated from one another by any inter-cellular substance, though the entire section is broken up into portions of unequal size by fibrous septa which traverse the tumour. These septa themselves are not numerous, and they are always very delicate. At the same time there is a great want of vascularity about the growth, but this is a feature which lympho-sarcoma has in common with lymphadenoma.

A further point of difference between lympho-sarcoma and lymphadenoma, but one which is not constant, and in any case is often difficult to make out, is that in lymphadenoma the enlarged spleen may show the presence of particles of yellow pigment in the trabecular meshwork; in lympho-sarcoma the spleen is not similarly affected.

Endothelioma.—Under the name **endothelioma** are included a number of tumours which ontologically belong to the class of sarcomata and yet, so far as their histological characters are concerned, have close resemblances to the carcinomata. By some authors they are included among the alveolar sarcomata, but of late years there has been an increasing tendency to collect them into a special group.

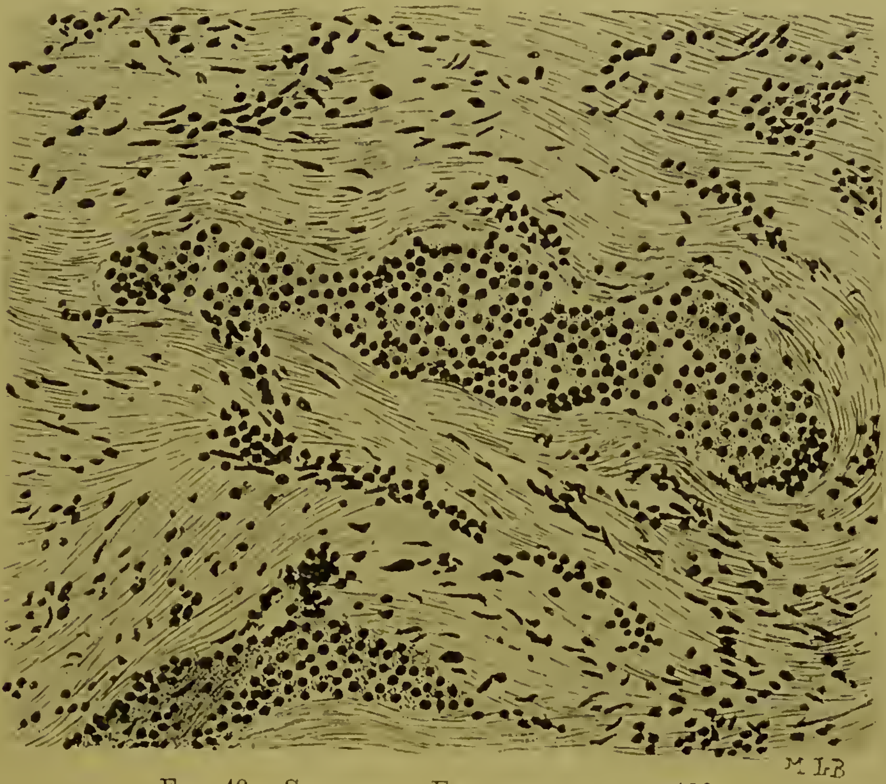

Fig. 49.—Section of Endothelioma. × 420.

From the dura mater. In the centre is a widely distended lymphatic filled with large endothelial cells having large round nuclei. A portion of a similarly filled lymphatic is seen below. Between these is a smaller lymphatic, which has undergone compression by the surrounding fibrous tissue, and recalls the lines of cells found in scirrhous carcinoma. Cf. figs. 55 and 56.

The endotheliomata, as their name implies, are composed of cells having the characters of endothelium; moreover they arise from normal endothelial cells, and as a result originate in structures in which these elements are present. The endotheliomata consequently are found to arise in connection with the serous membranes (peritoneum, pleura, dura mater), in connection with the lining membrane of blood-vessels and lymphatics, and in certain other situations where the explanation of their origin is more difficult.

If we consider the characters of an endothelial lining of a serous membrane such as the peritoneum, we shall recognise that the cells themselves are flattened, have a large amount of protoplasm relatively to the size of their nuclei, possess nuclei that are round or oval, and stain somewhat faintly with the ordinary basic dyes. In other words, they bear close resemblance to those cells of the blood which we speak of as 'hyaline cells.' Except for a cement substance these cells are in immediate contact with one another, not being separated by an inter-cellular substance, as is the case of cells belonging to the connective-tissue group generally. Thus endothelial cells have many analogies with epithelial cells, but it is now generally believed that they are not of epiblastic or hypoblastic origin, but are mesoblastic. It is by reason of this belief that the new-growths formed of endothelial cells are classed along with tumours formed by other members of the mesoblastic group, i.e. they are classed with the sarcomata, and not with the carcinomata, as their histological features would at first suggest.

Agreeably with their seats of origin the endotheliomata show a special tendency to be met with in lymphatics and in blood-vessels, especially those of a capillary type. The tumours also extend by means of these vessels, so that in a suitable case and at a suitable portion of the growth we can always discover in a microscopic section dilated lymphatics more or less completely filled with cells that are in contact with one another, and have the characters which have been described.

The actual appearance of an endothelioma varies considerably according as the parts which are under examination belong to the more or the less affected parts of the tumour. In the less affected portions—that is, towards the margin of the new-growth—we find a number of strands of cells arranged for the most part in lines parallel with one another and extending from the margin of the growth in a radial manner. These are the lymphatics crowded with the proliferating endothelial cells. In the more centrally disposed portions of the growth the cellular element predominates, and little connective tissue is visible. This depends upon the fact that the original elements of the part have vanished as the result of the pressure atrophy induced by the increasing numbers of endothelial cells.

It follows from what has been said in the last paragraph that the more central portions of an endothelioma are highly cellular, while the number of endothelial cells diminishes as one proceeds towards the periphery, owing to the greater persistence of the tissues which the endothelioma is invading. This arrangement of the growth is, as we shall see later, the exact converse of that which obtains with spheroidal-cell carcinoma of the breast, but so far as microscopical characters alone are concerned, there is the greatest resemblance between the hard (scirrhoid) portions of the mammary growth and the advancing edge of an endothelioma.

The endotheliomata are divided into two classes, the **lymphangeio-sarcomata** and the **hæmangeio-sarcomata**, though both of these are often collectively spoken of as **angeio-sarcomata.**

The lymphangeio-sarcoma does not call for special description here, as the general description of the endotheliomata that has already been given has been taken from a typical case of the lymphatic condition. It need only be added that the collections of endothelial cells may either form definite alveoli or solid cylinders of cells. In the latter case the cells sometimes undergo a form of hyaline degeneration, and then the variety of growth is produced which has been termed a **cylindroma.** As a matter of fact, it is probable that under the name cylindroma more than one variety of growth is included. Lymphangeio-sarcomata are most frequently met with in connection with the dura mater and the pleura. By far the largest number of the malignant tumours met with in the cranial cavity are of this nature. Both in the cranial cavity and in the pleura, endotheliomata form flat growths which extend mainly in the substance of the serous membrane itself; sometimes they extend for a short distance into the underlying tissues, but usually this only occurs to a slight extent. Lymphangeio-sarcomata are not very uncommon forms of new-growth.

Besides the situations in which these growths may be said to occur naturally, they are also met with rarely in other situations. Thus they are sometimes met with in the breast, and then they generally cause a considerable amount of difficulty owing to their resemblance to the carcinomata.

The hæmangeio-sarcomata are rare growths, but when one is seen it is generally recognised with ease. For the endothelial proliferation takes place in and along the walls of the small blood-vessels, and a picture is produced of a number of blood-vessels of small lumen with immensely thickened wall which consists of many layers of endothelial cells. These modified blood-vessels are separated from one another by a minute quantity of connective tissue, and if the vessels are well marked, and particularly if red blood corpuscles are to be found in their lumina, diagnosis is easy. If, on the contrary, the lumina are very small and are quite devoid of blood, the matter is more difficult, though even then the form of the 'alveoli' (as they are then probably thought to be) is so regular that the appearance of a microscopic section of the growth is unlike that of any other tissue or tumour. They are more commonly met with in the brain, the kidneys, testes, and mammæ than in any other situations, but even in these regions they are decidedly rare. Sometimes an ordinary angeioma of the skin takes on sarcomatous growth, and this variety of growth may be produced; angeio-sarcoma of the liver arising from a formerly simple angeioma is an excessively rare form of growth.

Distribution of the sarcomata.—Corresponding with their embryological seat of origin in the mesoblast, the distribution of the sarcomata is very widespread. They are met with most commonly, however, in the connective tissues and especially in connection with bone. Among the bones, long bones are far more frequently affected with sarcoma than short bones, but sarcoma of the bones of the tarsus, of the scapula, and of the bones of the skull is occasionally met with. Of all bones the femur, tibia, radius, and ulna are the most commonly affected; in them the growth is usually single, though secondary growths are formed in other parts. Sarcomata of the bones of the skull are often multiple.

Sarcomata also affect with frequency the soft organs, and here again we find that certain organs are far more frequently affected than others. Thus the heart is only with the greatest rarity the seat of a sarcoma, and even then it is almost always secondary; the testis, kidney, and ovary, on the other hand, are relatively often the seat of sarcoma. The thyroid body, too, is somewhat liable to be attacked by sarcoma, and the frequency with which lymphoid tissue is the seat of lympho-sarcoma has already been remarked.

Organs and tissues which have been derived largely from the epiblast and the hypoblast are, as one would expect, but little liable to be the seat of sarcoma. But it must be remembered that mesoblast enters into the composition of most tissues, though it may hold an inferior position, and that, in consequence, though it may be commonest for these organs and tissues to be affected by malignant growths of the epithelial type, it is not impossible that they should, at times, be affected with malignant tumours of the mesoblastic type. We have many excellent examples of this statement. Thus the breast is an organ derived from the epiblast so far as the true glandular portions are concerned, and consequently the malignant tumours of the breast are almost always carcinomata; but this does not exclude the fact that the mesoblast was concerned in the formation of the entire supporting structure of the organ, to say nothing of the blood-vessels, and therefore we meet, occasionally, with definite sarcomata in the breast, and in a few instances with true hæmangeio-sarcomata. The same is true in the case of the skin; the epidermal layers give rise to a carcinomatous growth, but sarcoma of the skin is not so very uncommon and arises in the corium, which is of mesoblastic origin. In the same way we occasionally find sarcomata of the tongue, the œsophagus, and the stomach, though the malignant growths of these parts are almost always carcinomatous.

The different kinds of sarcoma also have special seats of election. Thus the ossifying sarcoma is always primarily found in connection with bone, almost always in connection with a long bone, and more frequently in connection with the femur and the tibia than any other bones. Even in the case of the femur and tibia the entire length of the bone is not equally prone to attack by the ossifying sarcoma, for it is generally present at the lower end of the femur, and at the upper end of the tibia. This is true of all forms of sarcoma arising from the periosteum, and not of the ossifying variety alone. The myeloid sarcoma again shows certain differences. It has a tendency to affect bone of the most exclusive kind, but it differs from the spindle, round, osteo-, and chondro-sarcomata, in that it is an endosteal form of new-growth and not a periosteal. It affects the femur and the tibia like the others, but in addition it also affects the bones of the face with considerable frequency, constituting one of the commonest varieties of that form of new-growth which affects the alveolar margins of the jaws and is known as **epulis**.

So far as the remaining varieties of sarcoma are concerned, it is necessary to add but little to what has already been said. In the case of the internal organs one generally meets with small round- or small spindle-cell sarcomata. Mixed varieties are less common, and it is decidedly uncommon to find that the tumours are composed of cells of large size. The melanotic sarcomata always arise in connection with the skin (very frequently from some congenital mole or wart) or the choroid; psammomata are only seen in the brain, rhabdomyo-sarcomata hardly ever but in congenital sarcomata of the kidney, and glio-sarcomata are tumours of the brain. Endotheliomata, it has already been said, are met with in a variety of situations (most commonly, however, in connection with the cerebral membranes, the pleuræ, and the peritoneum), but wherever they are found they are connected intimately with the lymphatics or the blood-vessels of the part.

SECTION X

THE NEW-GROWTHS OR NEOPLASMS—continued

THE MALIGNANT TUMOURS

B.—The Carcinomata

Of equal importance with the malignant growths built up (for the most part) on the type of one or other of the connective tissues, are those malignant neoplasms which are composed of epithelial elements—the carcinomata. They are not less destructive to the tissues in which they lie or to life itself than the sarcomata, but they have differences in structure, in mode of dissemination, in the kind of tissue in which they are liable to occur, which render their separation from the sarcomata imperative. This is not to be taken as meaning that the two forms of growth are so sharply differentiated that they can never be confused with one another, for this is not the case. Reference has already been made to the great similarity which is borne by the endothelioma to the spheroidal-cell carcinoma, and in some cases the difficulty of arriving at a conclusion as to the actual nature of the growth is such that some authors have formed intermediate classes and speak of **sarcoma carcinomatodes** and **carcinoma sarcomatodes.** Though it must be allowed that such intermediate classes are undesirable owing to the facilities they afford for the shirking of a difficulty, there is no doubt that we meet with cases in which the epithelial elements are decidedly of a carcinomatous type, while the substance which lies between the alveoli of epithelial cells consists of connective-tissue cells that are of a typically embryonic or sarcomatous character. There is, of course, no reason why a reversion to an embryonic type should be confined to one element of a composite tissue alone, and consequently there is no inherent impossibility that growths may exist which partake of the characters of both the sarcomata and the carcinomata. Fortunately they are not of common occurrence.

The carcinomata, then, are epithelial growths in which the epithelial elements are carried in a supporting structure of adult connective tissue. Hence the growths are composite, for we must recognise that in a certain degree the supporting structure of the carcinoma is as definite a portion of the new-growth as the epithelial cells themselves. This is not the case entirely, however. For, as has already been said, the carcinomata, being foreign bodies, act as irritants, and ultimately lead to the formation of a connective tissue which is undoubtedly inflammatory. How far, in any given growth, the connective tissue belongs to the one type or the other, it is difficult to say.

The simplest way in which to describe the varieties of carcinoma is to distinguish them according to the nature of the epithelial cell which is concerned in their formation. We shall, therefore, describe separately the squamous, the columnar, and the spheroidal carcinoma.[1]

(*a*) **The squamous-cell carcinoma.**—This variety of carcinoma is met with in regions which are normally covered by an epithelium of the squamous kind. It is therefore seen most frequently on the epidermis, or, to be more exact, at some point where there is a transition from the cutaneous epidermis to an epithelium. Thus we meet with squamous carcinomata of the lips, the tongue, the tonsils, the pharynx, larynx, and œsophagus, all of which parts are covered by a squamous epithelium. Continuing along the alimentary tract, we fail to find this variety of carcinoma until we reach the anus, but here again, where the epithelium of the intestinal tract passes into the squamous epithelium of the surface, squamous carcinoma is common.

In the case of the genito-urinary tract, squamous carcinoma is only met with in the male about the meatus urinarius, but a carcinomatous condition of the glans penis is not an uncommon form of disease. In this region carcinoma has certain points of difference from squamous carcinoma in other situations; to these we shall refer when dealing with the diseases of the male generative organs. Carcinoma of the scrotum is really nothing more than a carcinoma of the skin affecting a special region. In the female, carcinoma, generally, of the generative organs is far commoner than it is in the male, and a squamous carcinoma of the cervix is by far the commonest of all forms of carcinoma affecting the generative organs in both sexes. Carcinoma of the external genitals in the female is moderately common, and it is almost always of the squamous variety.

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[1] In the present work a term which has often been applied to certain of the carcinomata—viz. epithelioma—is entirely discarded. This term is used by many authors in England and France in connection with carcinomata composed of squamous or of columnar cells, so that the expressions 'squamous epithelioma' and 'columnar epithelioma' are often heard. In Germany the same rule holds good to a considerable extent, but Ziegler has employed the term in his text-book in a different sense. He now uses it to indicate non-malignant growths composed of epithelial elements, so that he speaks of the callosity and the wart as epitheliomata. No doubt this plan is in reality the best, for it brings epithelial growths into a line with growths composed of other kinds of elemental tissue. In this country, however, such use of the term would be very inconvenient, owing to the fact that we cannot conceive of a non-malignant 'epithelioma.' It is for these reasons that it has been decided to discard the term. Its omission is the less to be regretted in that students are exceedingly prone to think that there is some essential difference between the 'carcinomata' and the 'epitheliomata.'

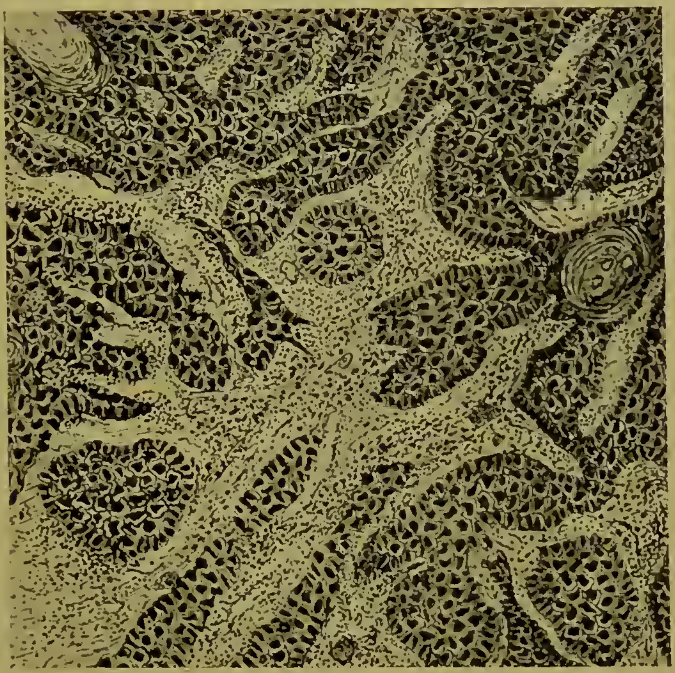


FIG. 50.—SECTION OF SQUAMOUS-CELL CARCINOMA. × 300.

The epithelial processes show a fairly regular layer of cells (Malpighian layer) next to the fibrous-tissue stroma. Internally the cells are polygonal from mutual pressure, and show spaces between the nuclei. It is in these spaces that the 'prickles' of the 'prickle cells' are to be sought. Close to the right-hand margin and in the left upper corner are 'cell nests.' In some cases the epithelial processes are cut at right angles, and therefore appear circular.

Whenever a squamous carcinoma has reached any considerable size, it invariably degenerates in the central parts. This degeneration is fatty, in part, but more particularly it consists in a molecular necrosis. As a result a squamous-cell carcinoma always shows an ulcerated surface, and this, being situated in the midst of a tissue which consists of a number of closely packed cells contained within alveoli separated from one another by newly formed connective tissue, presents ragged and hard edges. In some cases the edges grow up around the ulcer with the production of a number of excrescences which conceal, in some measure, the floor of the ulcer and cause the appearance of a 'cauliflower' growth. In other cases, of which the so-called 'rodent ulcer' is an example, the ulceration proceeds to such an extent that only a small portion of the growth remains to encircle and lie beneath a large ragged ulcer.

The histological characters of the squamous carcinomata are well marked. If we examine a portion of such a growth taken about its centre, we shall find that it consists of a number of solid processes of cells which ramify in all directions (but never anastomose), and which are separated from one another by a varying, but usually small, amount of well-formed connective tissue which carries blood-vessels for the nutrition of the growth. In the centre of the growth it is often difficult to make out the actual nature of the cells of which it is composed, for the cells themselves are in a large measure crowded out by the presence of cell nests (cf. *infra*), or have undergone degeneration as the result of mutual pressure.

In the peripheral portions of the tumour, whether they lie superficially or in the depth of the tissues, the structure of the tumour is more readily to be made out. It is then seen that the elements are those of the normal skin arranged in the same fashion with regard to one another so far as the actual layers composing the epidermis are concerned, but without the same regularity. At the very edge of the tumour the commencement of the process can be observed, for it is seen that there is a downgrowth of the inter-papillary processes of epidermal cells. This downgrowth takes place into the corium at first, but soon the epithelial processes pass beyond the corium and invade the tissues that lie beneath it. A cross section of one of the epidermal downgrowths therefore is round or oval, and it shows at the periphery a more or less regular layer of cells arranged radially, and somewhat elongated in shape (corresponding to the germinal layer). Internally, this is succeeded by layers of prickle cells which, becoming flattened as they progress towards the centre of the epithelial process, approximate more and more to the characters of the keratinous layer of the skin. In squamous carcinomata which have originated in portions of the cutaneous epithelium, a representative of the stratum granulosum is also to be made out by the presence of cells in which eleidin granules may be found in quantity. In squamous carcinomata that have arisen from portions of an internal squamous epithelium, this layer is wanting.

The keratinous layer of skin is usually well represented in squamous carcinomata, but it does not form a continuous layer as under normal conditions. It is represented by the formations known as **cell nests** or **epithelial pearls**. As their name suggests, cell nests consist of a number of epithelial cells arranged in a special fashion. In the centre are usually two or three cells of large size with well-marked nuclei and often vacuolated; around these are flattened epithelial cells arranged in an imbricated manner, the cells themselves being more numerous and more flattened as one approaches the outer margin of the nest. The entire formation has therefore, in section, an appearance very like that of an onion cut through the middle, transversely. The cells entering into the formation of a cell nest are nucleated and the nuclei, like the cells themselves, are flattened. The entire cell nest possesses the tinctorial properties of keratin, so that, for example, it stains a brilliant yellow with picric acid. The nuclei, however, usually retain the property of staining with basic dyes, and are very conspicuous features of the cell nest.

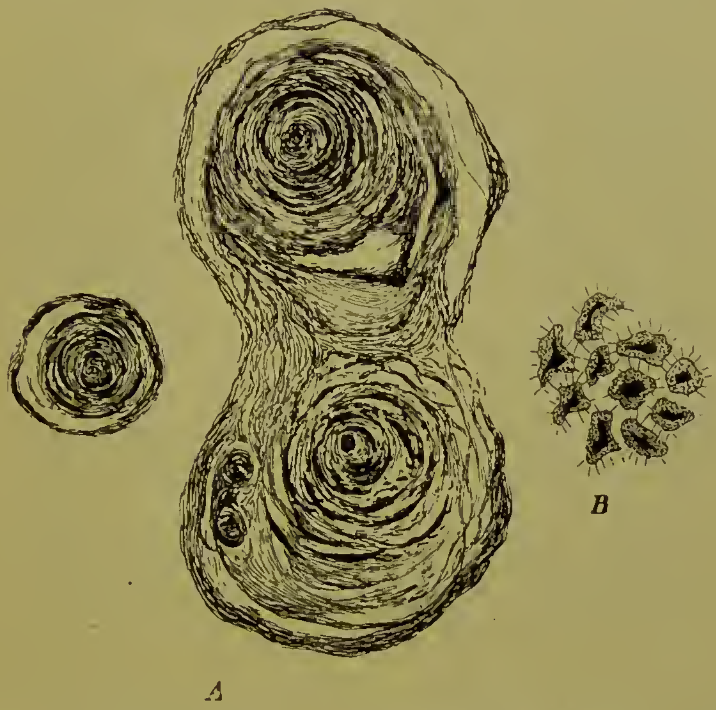


FIG. 51.—(*A*) 'CELL NESTS' AND (*B*) PRICKLE CELLS FROM A SQUAMOUS-CELL CARCINOMA. × 180.

A simple and a compound cell nest are shown. The prickle cells are semi-diagrammatic.

Cell nests, in their typical form, are spheroidal, so that they present a circle whichever way they are cut in a section. But, though this is the typical form, divergences are very common.

Thus we often find oval cell nests, and in a specimen of squamous carcinoma rich in cell nests, it is often impossible to say more than that the boundaries of the cell nests are curvilinear. The reason of this is that there is a great tendency for adjacent nests to coalesce, and consequently it is common to find that a cell nest consists of a double, triple, or even multiple, centre which is surrounded by a few layers of concentric flattened epithelial cells. In any case the keratinous nature of the cells remains. Reference has already been made to the absence of a stratum granulosum in the squamous epithelium of an internal surface; cell nests found in squamous carcinomata derived from an internal squamous epithelium show the same characteristic.

The number of cell nests found in specimens of squamous carcinoma varies considerably. In some they are so numerous that they almost obscure the other features of the growth, in others they are only to be found after prolonged search. As examples of these statements squamous carcinomata of the tongue and of the cervix may be mentioned. In the case of the tongue it is usual for cell nests to be numerous, large, and well formed; in the case of the cervix, cell nests are commonly few, small, and ill formed, so that it is often a matter of doubt whether the formations seen are cell nests at all. These examples, however, are subject to many exceptions, but it may be said with certainty that when cell nests are found in a microscopic section, they afford very strong presumption that the material from which the section was taken was a carcinoma of the squamous type. It is necessary to make one reservation, however. Cell nests of a perfectly typical appearance are sometimes to be met with in the mucous membrane of the mouth and pharynx even when it is quite normal. The tonsils, too, are a rather favourite situation for them. But this hardly disturbs the fact that they predominate so considerably in cases of squamous carcinoma that they may, for all practical purposes, be taken as diagnostic of the condition.

Owing to the rapidity with which the epithelial cells of a carcinoma proliferate, the prickle cells in a squamous carcinoma are particularly well marked in many parts of the tumour. The same is true in the case of the simple papilloma.

Rodent cancer.—In close connection with the squamous carcinoma it will be convenient to describe a form of carcinoma which has many similarities with squamous carcinoma, but has equally many points of difference. The growth in question is an undoubted carcinoma, although the name rodent 'ulcer' has been long used to describe it.

Rodent cancer is a form of new-growth in which the chief characteristic is that the growth shows a marked tendency to the destruction of tissue locally without a corresponding tendency to the formation of metastases in the neighbouring lymphatic glands. Local removal, therefore, if complete, leads to a complete cure, and in this respect rodent cancer is in marked contrast to the carcinomata generally, and in particular to squamous carcinoma. The local destruction brought about by extension of the growth is considerable, however, and resistless (apart from complete removal of the growth), so that in a neglected case the whole of one side of the face may be destroyed and a foul cancerous ulcer take its place.

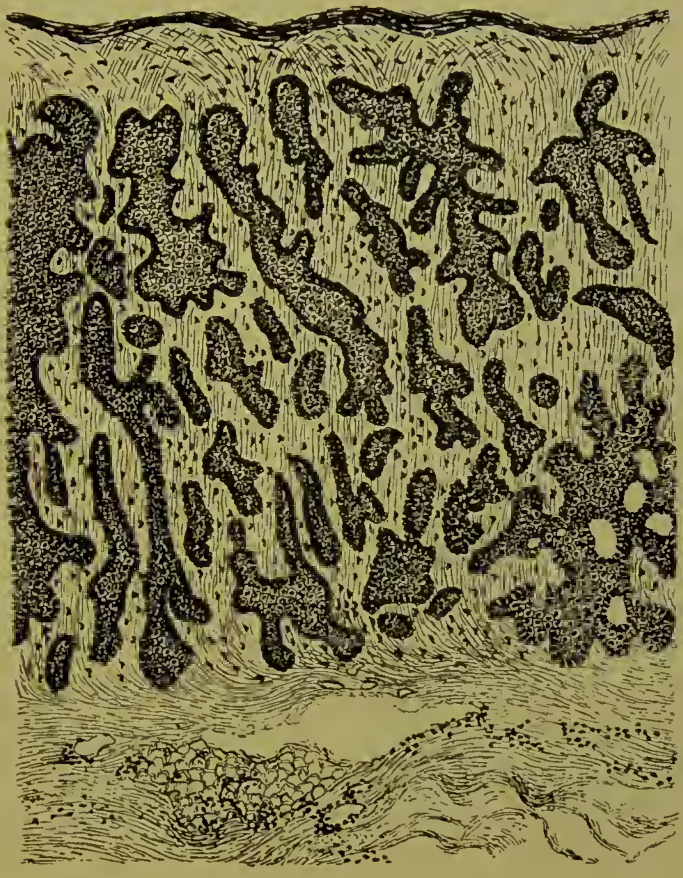


FIG. 52.—SECTION OF RODENT CANCER. × 320.

Above is the epidermal layer (dark); beneath is the fibrous tissue corium infiltrated with numbers of irregular epithelial processes. Note that no cell nests are present. At the bottom of the figure is subcutaneous fatty tissue.

Rodent cancer shows a special tendency to affect the face in the neighbourhood of the outer canthus of the eye, but it may be met with anywhere on the face. On other parts of the body it is decidedly rare.

The histological characters of rodent cancer are fairly definite, but it is at times difficult to decide whether the section has been taken from a case of this form of malignant disease or from a squamous carcinoma. The reason of this is that the rodent cancer consists of a number of epithelial prolongations into the corium and still deeper tissues. The microscopic resemblance between these prolongations and those occurring in squamous carcinoma are considerable, for in both varieties of growth we have cross sections of a number of irregular epithelial processes separated by a small amount of connective tissue. But it is generally possible to distinguish between the two varieties of growth by the shape of the cells and of their nuclei, by the shape of the cross sections of the solid processes of cells, by the presence or absence of cell nests, and by the appearances of the epithelial lining of the hair follicles and sebaceous glands.

Unlike the squamous carcinoma which arises from ordinary squamous epithelium, the rodent cancer seems to arise from that special variety of squamous epithelium which passes down the hair follicles, and therefore forms a lining for them, and extends along the ducts of the sebaceous glands as far as the glands themselves. The cells of which this form of epithelium is composed are smaller than the cells of a cutaneous epidermis, their nuclei are more regular, smaller, and more oval in shape. These features characterise the cells contained in the solid processes which invade the deeper tissues in rodent cancer, and the cross sections of the processes have a somewhat different appearance from those of the solid processes of epithelium in a squamous carcinoma, being smaller, more angular, and more equal in size. At the same time the solid processes of a rodent cancer show a much greater tendency to branch.

The epithelium about the hair sacs and the sebaceous glands in the immediate neighbourhood of a rodent cancer is the seat of a marked proliferation, and an extension of this proliferated epithelium into the deeper tissues may often be seen. It is on this account that it has been supposed by many authors that the rodent cancer consists in an invasion of the tissue by epithelium derived from this source. It is certainly probable that some other form of squamous epithelium than that which forms the ordinary covering is concerned in the process, for in addition to the differences between the shape of the cells, &c., which have already been noted, the rodent cancer is devoid of those cell nests which are so characteristic a feature of the squamous carcinoma. It must be conceded, however, that it is possible that the changes in the epithelium about the hair sacs and the sebaceous glands may be secondary and not primary in the history of the growth.

(*b*) **The columnar cell carcinoma.**—This variety of carcinoma is met with in regions which are provided normally with a columnar epithelium. It is, therefore, commonest in the intestine and in connection with the excretory ducts of glands.

In the alimentary tract a columnar carcinoma is practically never found between the lips and the lower end of the œsophagus. Even in the stomach it is much less common than the spheroidal cell carcinoma, but it nevertheless occurs. When one has passed the pylorus, columnar-cell carcinoma becomes the especial form of malignant disease met with in the intestine, down to the anus, where it gives place to carcinoma of the squamous variety. The intestine is not equally liable to the occurrence of carcinoma in its entire length, for carcinoma of the small intestine is very rare, while the large gut is frequently affected. The chief situations at which malignant disease of the large intestine occurs are the rectum, the sigmoid flexure, the splenic flexure, and lastly the hepatic flexure of the ascending colon. Carcinoma of the cæcum is rare, and of the ileo-cæcal valve excessively rare.

The order of frequency with which different parts of the large gut are the seat of carcinoma is the order in which the parts have been mentioned above, and it is noteworthy that the frequency with which malignant disease is met with increases as one passes down the gut—that is, it increases according as the fæces become more solid. This fact is an important argument in favour of the view that carcinoma is the result of mechanical factors.

In connection with the excretory ducts of glands columnar carcinoma may be met with in any situation, but the commonest is certainly the breast, where it gives rise to a somewhat special variety of growth known as duct carcinoma. To this variety reference will be made later.

In a measure it may be said that the carcinoma which is met with in the intestine has developed from the columnar epithelium lining a duct. For the tubular gland is the simplest form of a gland provided with a duct, and in it the secreting and the conducting portions are only imperfectly divided. Or rather, with the exception of the few polygonal cells at the fundus of the gland, the conducting portion is also the secreting portion.

Bearing this fact in mind, it is easy to understand how the columnar-cell carcinomata have analogies with the tubular adenomata, and also how we meet with carcinomata that are, so to speak, lined by an epithelium that is transitional between true columnar and true spheroidal epithelium. In the latter instance it is sometimes quite impossible to decide whether the growth should be regarded as a columnar- or as a spheroidal-cell carcinoma. This is particularly the case with regard to carcinomata of the stomach.

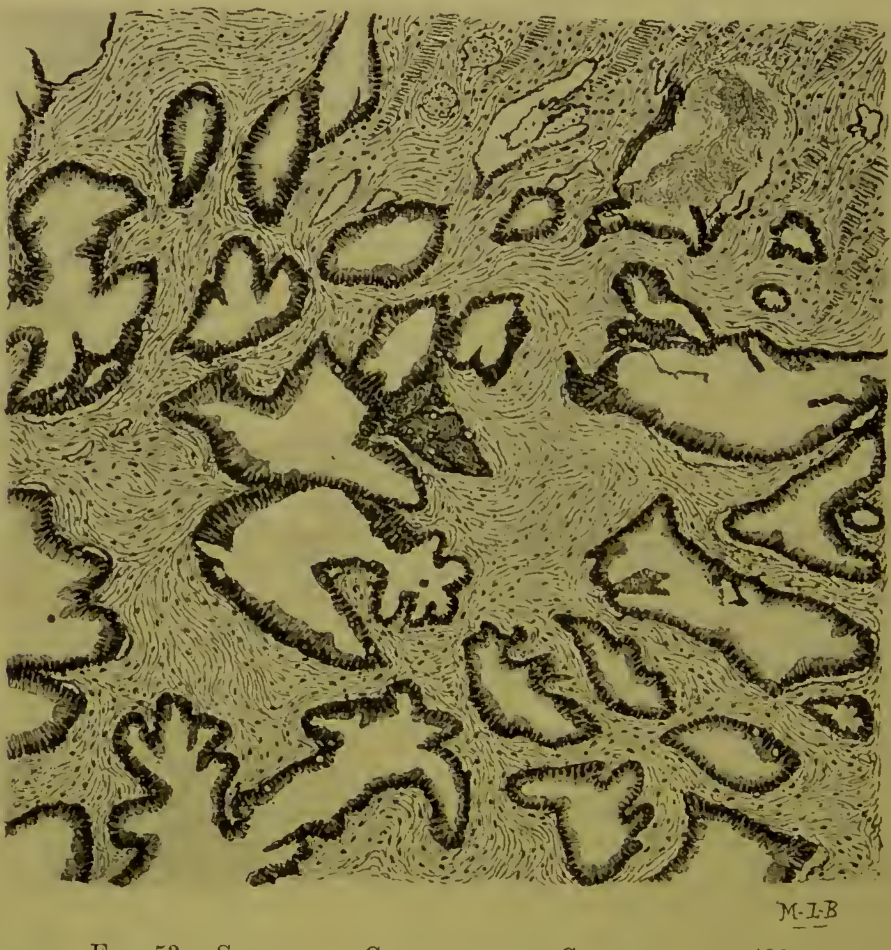


FIG. 53.—SECTION OF COLUMNAR-CELL CARCINOMA. × 480.

From the intestine. In a stroma of fibrous tissue are irregular duct-like formations lined by a single layer of columnar cells; in some places goblet cells are seen. Above are a few strands of the muscular coat of the intestine, which the growth is invading.

Macroscopically, columnar-cell carcinomata form tumours of different sizes. They are rarely very large, owing to the importance of the parts which they affect, in the first place, and in the second owing to their tendency to undergo local necrosis and form a malignant ulcer. The growths themselves are usually fairly hard in consistency, and in the case of the gut they generally form a ring around the part which leads to a definite stenosis. Although the stenosis is never absolute, in a large number of cases the lumen which is left is not larger than will just allow the tip of the little finger to pass. However, the obstruction to the passage of fæces is complete, and the ultimate symptoms to which the condition gives rise are those of acute intestinal obstruction. In the mamma, the growths are often of fair size, and they do not tend to break down on the surface so much as some other varieties of carcinoma.

Microscopically, the columnar-cell carcinoma consists of a number of irregular alveoli or tubes lined by a layer of columnar epithelium which is often extremely regular, though in places there may be seen a tendency to the proliferation of the epithelial cells. These alveoli are supported by a connective tissue which is usually very scanty in amount. Except in their irregularity of shape there is little in the alveoli themselves to indicate that the growth in which they are present is malignant. It will, however, be noticed that the alveolar portions are not confined to the normal limits. For example, in the intestine they are not bounded by the muscular layers but invade, destroy, and replace them. It is in this fact that the malignancy of the columnar-cell carcinoma consists, and were it not for this feature it would be practically impossible to distinguish under the microscope a columnar-cell carcinoma from a focus of hyperplasia of tubular glands in a region the seat of a chronic inflammation. Such a distinction is in many instances impossible to make. Thus it is often desirable to know whether portions of the endometrium removed by curetting are derived from a uterus which is the seat of chronic inflammation, or from one which is the seat of columnar-cell carcinoma. Without evidence as to the question whether such irregular glands as may be found have invaded the body of the uterus or not, it is impossible to give a definite opinion.

Since the alveoli of a columnar-cell carcinoma are provided with a central lumen, it might be expected that we should occasionally meet with the occurrence of papillomatous prolongations of the wall into the lumen. This actually occurs, and we meet with varieties of columnar-cell carcinoma that are distinctly villous. In most instances the lumen of the alveolus is dilated to an extent that may fairly be called cystic, and the growths thus constituted are sometimes spoken of as *proliferating* or *papillomatous cystadenomata*. The term is useful in the respect that it emphasises the chief characters of the growths, but it is disadvantageous in that it separates these growths from the columnar carcinomata generally. It must be conceded that the villous carcinomata have certain peculiarities which divide them to some extent from the ordinary columnar-cell type; they do not show quite the same tendency to infiltrate the tissues in which they are situated, but rather push them on one side, and they also have a special tendency to affect the kidney, the testis, the ovary, and the breast. But so far as the characters of the cells of which they are built up are concerned, their tendency to form secondary deposits and to destroy life, they do not differ from other varieties of the malignant growths. It is better, therefore, to speak of them as columnar carcinomata, prefixing the attribute **villous** to which they have a just claim.

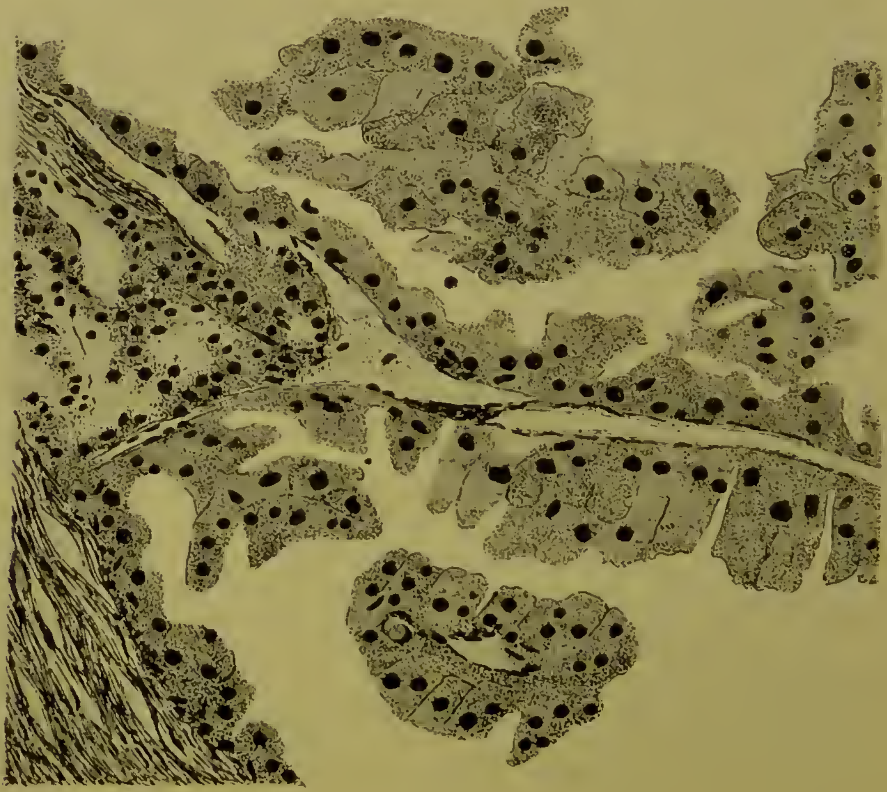


FIG. 54.—SECTION OF PAPILLOMATOUS CYSTADENOMA. × 480.

From a secondary growth in the liver, primary growth in the kidney. From the connective-tissue stroma (left) a process runs across the figure, carrying a blood-vessel and lined by a layer of large columnar cells with round darkly staining nuclei. Above and below are portions of processes that were running at right angles to the plane of the section.

In the case of the breast, the villous columnar carcinoma has received the distinctive name of **duct carcinoma**. It is certainly the most obvious form in which we meet with columnar carcinoma in this organ, but it is doubtful whether it is the sole representative of the class. Some authors have held that columnar carcinoma is of frequent occurrence in the breast, and it has even been held that the majority of mammary carcinomata are of this type. There is little doubt, however, that this is not the case.

Duct carcinoma is not only different in its histological appearances from the ordinary carcinomata of the breast; it also differs in macroscopical features, owing to the presence in it of small cysts in which the presence of intracystic papillomata may usually be seen with ease. It is, in addition, important in that it is less malignant than the other forms of mammary carcinoma, owing to its smaller tendency to affect the lymphatic glands.

In the kidney, villous carcinomata are met with relatively often as a form of malignant new-growth, and given that the growth is a carcinoma, it is more commonly of this type than of any other. In the kidney, and also in the testis and ovary, the cysts themselves are usually of considerable size, but the intracystic papillomata are so numerous and their branching is so great that the tumour may not appear to be cystic at all to the naked eye. The secondary growths in this, as in the other forms of columnar carcinoma, reproduce the characters of the primary growth.

(*c*) **The spheroidal cell-carcinoma.**—This variety of carcinoma is composite like the other varieties, in that it consists of a connective-tissue framework which carries blood-vessels, and an alveolar portion which is lined by epithelial cells. In this case, however, the type of the epithelial cell is different, for it is one which normally proliferates and breaks down into the secretion.

The true secreting portion of a typical gland consists of an alveolus containing a number of spheroidal, cubical, or polygonal cells, which are formed internally to the basement membrane of the gland, and ultimately break down to form the specific secretion of the gland. In the spheroidal-cell carcinoma, this essential function of the gland cell is generally in abeyance, so that there is no formation of the secretion. In some cases, however—e.g. carcinoma of the thyroid body—a substance is present which must be looked upon as the representative of a secretion. In the instance mentioned coloid is formed. But in any case the fundamental fact underlying the formation of the secretion, viz. a multiplication of cells, still remains. As a result the alveoli probably become filled with cells of the spheroidal type.

The atypia of the condition is manifested further. For not only do the individual cells generally depart from the usual type so far as function is concerned, but also the alveoli themselves, considered as composite factors, are different. They no longer maintain an orderly arrangement and shape, but they run riot, so to speak, and, as solid processes of cells, thrust themselves into the tissues in all directions without reference to what were formerly the true confines of the gland. It is because of the manifest resemblance of this form of carcinoma to a normal secreting gland, and its constant liability to originate in secreting glands, that it has been termed the glandular carcinoma.

If a portion of the soft part of a spheroidal cell carcinoma is scraped and a suspension of the cells which are thus obtained is made, it will be found upon examining a little of the suspension under the microscope, either stained or unstained, that the cells are very variable in shape, of large size, contain a large nucleus, and often a highly granular protoplasm. The shape of the cells is so variable that it is almost impossible to say that any one form is the typical; upon the whole, they are devoid of processes, and the name 'spheroidal' best describes them. Such variations in shape as are observed are evidently the result of mutual pressure. The nuclei are large and round, they often show a well-marked nuclear network and almost always one or more well-defined nucleoli. It is not uncommon either for signs of cell division to be manifested. In such cases we generally meet with two or perhaps three fully formed nuclei in the cell, but sometimes definite karyokinetic figures are to be seen.

In microscopic sections the appearances of the cells are different, and in particular the cells do not look so large as they obviously are when examined in a scraping. Neither is their granular character, nor the outline of the cells themselves, nor the shape of the nuclei, so well to be seen. But, on the other hand, the characters of the composite growth are readily recognisable.

If we take a mammary carcinoma as a fair example of a spheroidal-cell carcinoma, we shall find that the appearances presented are different according as we examine the central or the peripheral portions of the growth. In the peripheral portions there are numerous alveoli of large size filled with cells which show only a moderate quantity of protoplasm, but contain large nuclei that stain deeply. The cells are packed tightly in the alveoli, and it is impossible to distinguish the presence of any material between individual cells. The alveoli themselves are of varying size, but they are, for the most part, round or irregularly polygonal. Between them there is a small amount of connective tissue of the ordinary type which carries blood-vessels for the nutrition of the growth. In advance of the alveoli there is a narrow zone of small round cells that are obviously leucocytes, and are, in the majority of cases, indistinguishable from lymphocytes or small hyaline cells.

In the more central portions of the growth the picture is different. For here the principal constituent of the tumour is dense fibrous tissue of a cicatricial type, and such cells as are present are few in number, collected into small groups, and greatly compressed by the contraction of the fibrous tissue. The remains of the carcinoma cells in this portion of the tumour possess a somewhat special appearance. For, owing to the fact that the connective tissue is arranged in a more or less radial fashion, the cells themselves are compressed between more or less parallel lines. As a result they lie in columns in which the cells are placed either in Indian file or are arranged two or three abreast. Alveoli in the strict sense of the term are absent, and

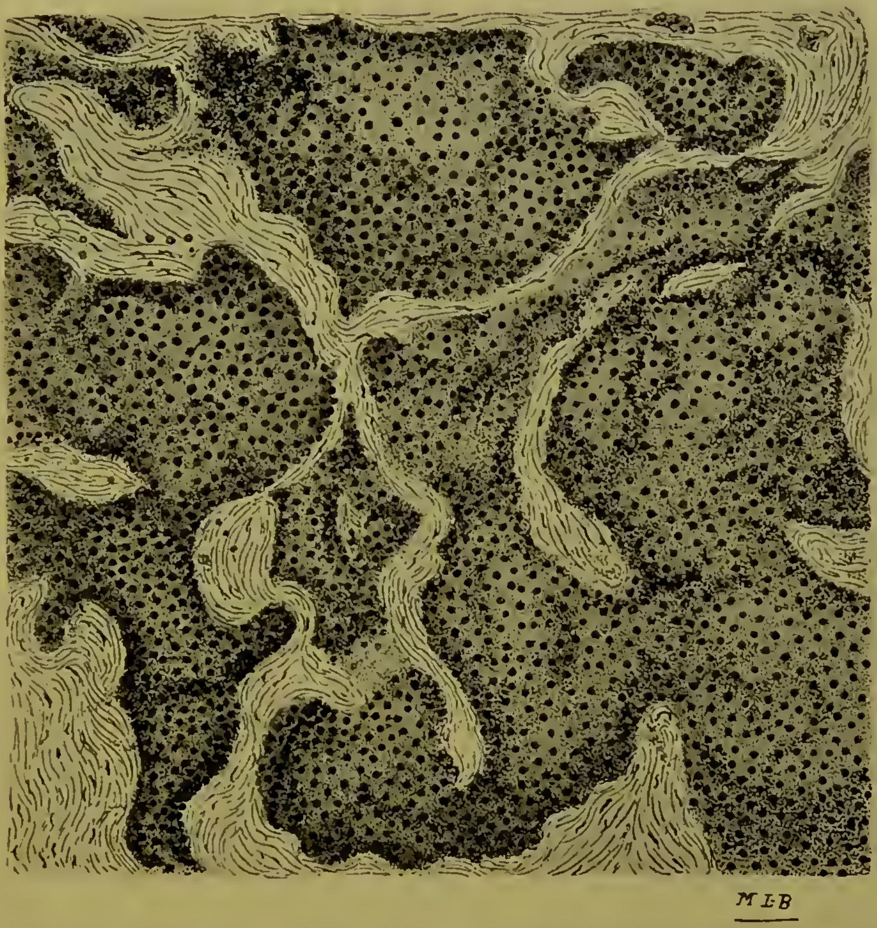


Fig. 55.—Section of Spheroidal-cell Carcinoma (Soft Part). × 480.
From the breast. The irregular masses of spheroidal cells with large round nuclei are separated from one another by bands of fibrous tissue. The outlines of the cells themselves are not seen in sections.

the cells appear to lie in lymphatic spaces. Whether the lymphatic spaces are really the pre-existing lymphatic spaces of the breast, or whether they are newly formed, it is impossible to say. The dense portion of the growth is often termed a **scirrhus**, while portions having the characters of the peripheral portions, from their similarity in consistency to brain substance, are sometimes termed **encephaloid**, but this term is not so much used at the present day as it was formerly.

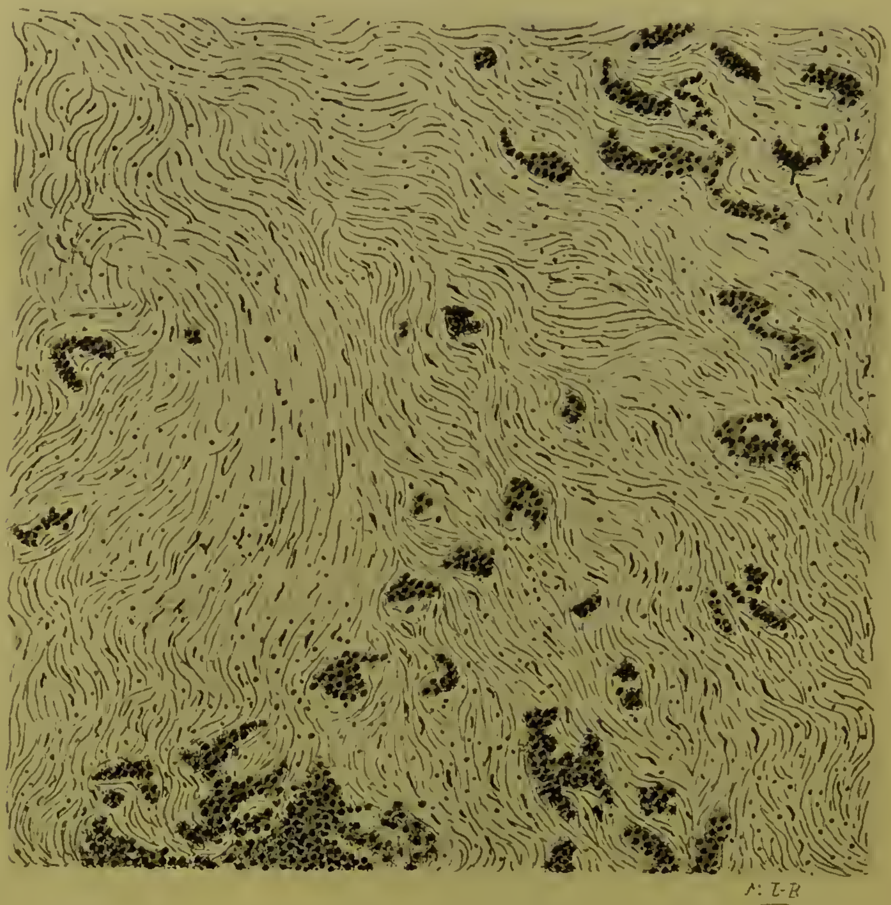


Fig. 56.—Section of Spheroidal-cell Carcinoma (Hard or 'Scirrhous' Part). × 480.

From the same case as fig. 55, and in the centre of the growth. The tissue is very dense fibrous tissue, for the most part free from epithelial cells. In the right-hand corner are strands of epithelial cells formed by compression, and below are larger masses similar to those in fig. 55.

At the edge of the growth it is always possible to see evidences of the process by means of which the normal tissues are destroyed in advance of a growth. For the essential cells of the part are definitely compressed, the cells are atrophied and shrunken, while fingerlike processes of the growth insinuate themselves into the normal tissues in every direction. By means of these processes the growth extends far beyond its macroscopic limits, and as the processes extend along the lumina of lymphatic channels, the means are afforded whereby that affection of the lymphatic glands which is so characteristic a feature of the carcinomata is made possible.

In the breast we usually meet with both the hard and the soft forms of spheroidal cell-carcinoma, but in other regions one form is generally present to the exclusion of the other. Thus in the case of spheroidal-cell carcinoma of the stomach we meet with the soft form when the cardiac end of the organ is affected, but the scirrhoid form in carcinoma of the pylorus. But whatever the type of the primary growth the secondary growths are always of the highly cellular variety. They tend, also, to be more definitely circumscribed than the primary growth, and although it is easily seen under the microscope that they are

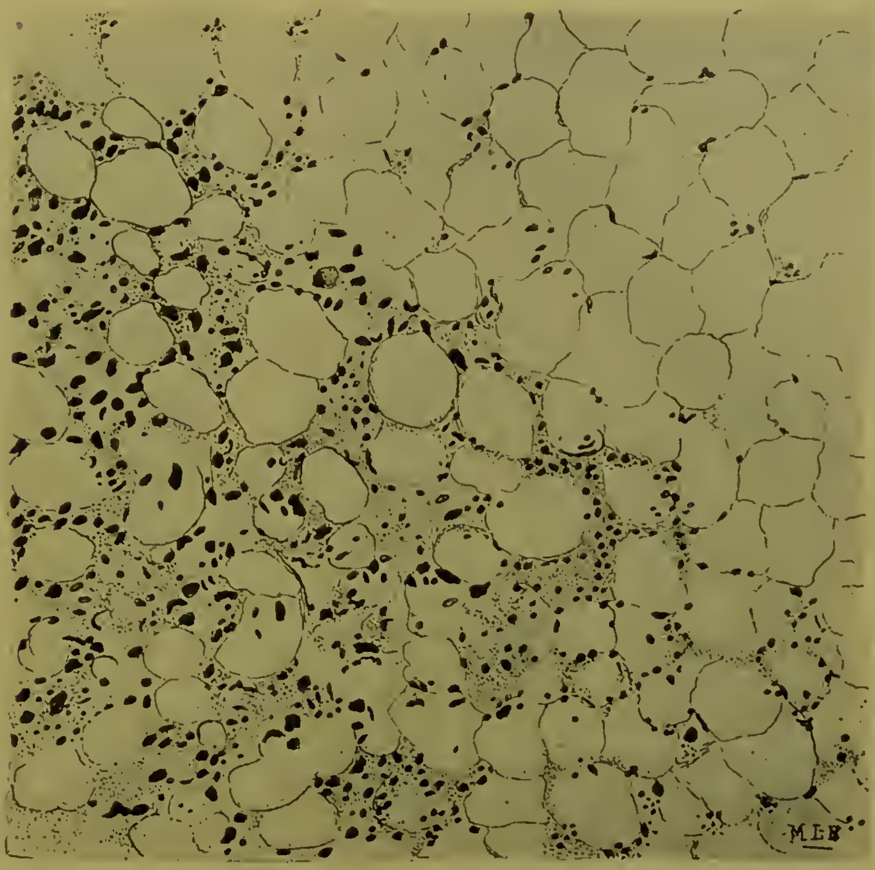


FIG. 57.—SECTION OF SPHEROIDAL-CELL CARCINOMA (GROWING EDGE). × 480.

From the same case as figs. 55 and 56. The carcinoma is invading fatty tissue (fat globules removed in preparing the paraffin section). The large nuclei are those of epithelial (cancerous) cells, the small nuclei are those of leucocytes forming the 'small cell infiltration.' Note the complete absence of encapsulation.

not encapsuled but encroach upon the surrounding tissues and invade them in a manner comparable with that which obtains in the case of the primary growth, there is no doubt that a sharper line can be drawn between the normal tissues and the tumour in the case of the secondary growths than can be done in the case of the primary.

As a special subdivision of the spheroidal-cell carcinoma mention must be made of that form of carcinoma in which an extensive colloid degeneration of the epithelial cell takes place. **Colloid carcinoma** is not of very common occurrence, but when it is met with the degeneration is usually so extensive that but little of the epithelial structure of the cancer persists. In its place the alveoli are filled with a material of homogeneous appearance and consistency which gives the characteristic staining reactions of colloid.

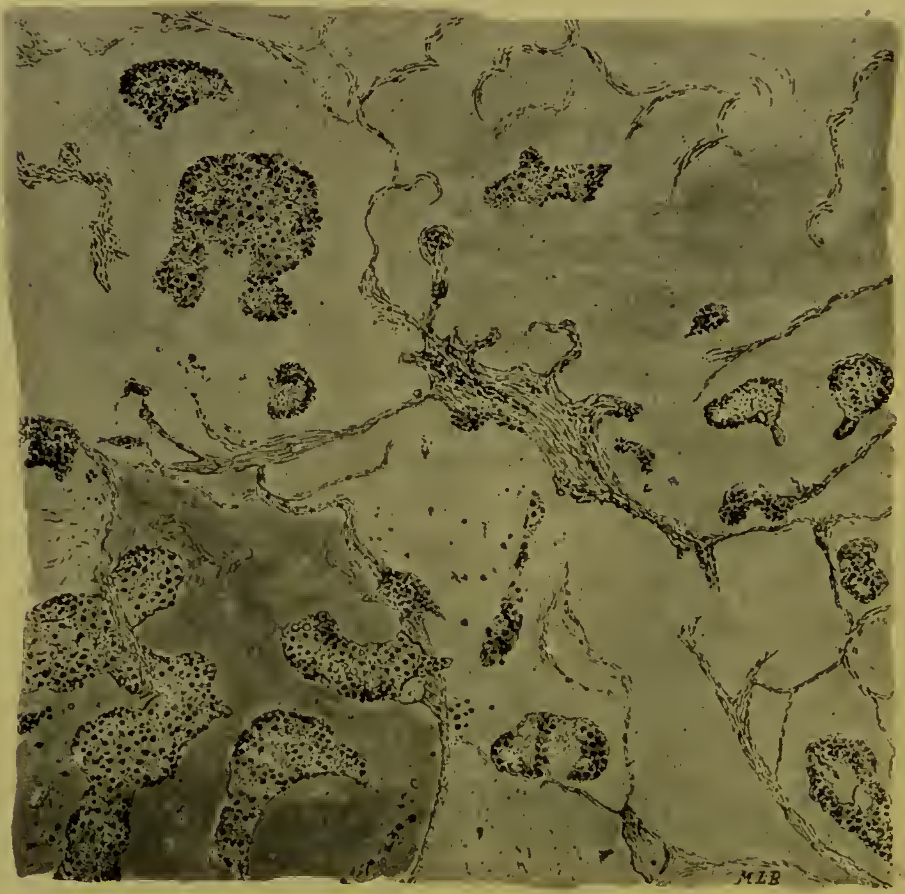


Fig. 58.—Section of Colloid Carcinoma. × 60.

From the breast. Very few cancer cells are present, but the spaces between the fibrous trabeculæ are filled with homogeneous colloid material. Islets of spheroidal carcinoma cells persist chiefly in the centres of colloid masses.

If a large series of sections covering a considerable portion of a colloid carcinoma are examined microscopically, it will be seen that the statement that the alveoli are filled with colloid material and the epithelial cells are almost wanting needs some modification. For, though it will be evident that the greater number of the epithelial cells have undergone the colloid change, it will be found that at the margin of the growth the tumour is cellular and has appearances like those of an ordinary spheroidal-cell carcinoma. A little more centrally alveoli will be found in which a certain number of the cells are metamorphosed, while the remainder are of normal appearance and stain ordinarily. In these alveoli the normal carcinoma cells may lie at the periphery of the alveolus, or may lie in the centre of a mass of colloid material. More centrally still the amount of colloid becomes greater while the number of unaltered cells diminishes. But although in the centre of the growth it is a fact that a large number of the alveoli are filled with colloid material to the complete exclusion of epithelial cells, one can always find foci where a few cells remain which appear to have entirely escaped the degenerative process.

Colloid carcinoma is almost always of the spheroidal type. It occurs chiefly in the case of carcinomata of the alimentary tract and the breast. The pancreas also is sometimes affected with this form of cancer.

As might be expected, colloid carcinoma is less rapid in its growth than those forms of carcinoma in which the cellular element strongly predominates. For the same reason its malignancy is also less. The secondary growths in a case of colloid carcinoma are generally few in number, and though they may also show the colloid change, it is not uncommon for them to be of the ordinary cellular type. Very occasionally numerous minute secondary growths are found (*e.g.* in the lungs), the centres of which are completely converted into colloid. In such a case the condition may be mistaken for miliary tuberculosis until the microscope reveals the true nature of the nodules.

SECTION XI

CYSTS AND CYSTOMATA. DERMOID CYSTS

In this section we are about to consider a number of different conditions which have, however, one point in common. They all are characterised by the fact that they form swellings in whole or in part, that these swellings are entirely or partly of fluid or semi-solid consistency, and that these fluid or semi-solid substances are contained within cavities bounded by definite walls.

In some cases these swellings are not tumours in the strict sense of the word, but in others the entire growth is a true tumour. For this reason the swellings have been divided into the two classes, **cysts** and **cystomata**. Another method of dividing them is into *true* and *false* cysts.

(*a*) **Cysts.**—A cyst is in the majority of cases a collection of fluid, but all collections of fluid are not termed cysts. Thus an abscess is a collection of fluid, but the term 'cyst' is never applied to it; so, too, we meet with accumulations of fluid in the peritoneal and pleural cavities, but here again the term 'cyst' is never used in connection with them.

Cysts are formed in a variety of ways. The commonest depends upon the closure of a duct and the accumulation behind the obstruction of a fluid derived from the tissues to which the duct normally acts as an outlet. In a large majority of cases this tissue is glandular, and thus we meet with cysts in connection with the submaxillary gland (ranula), in which the contents of the cyst are a somewhat modified salivary secretion. Pancreatic cysts are of a like formation, and depend upon obstruction to Wirsung's duct. In these cases we have to deal with definite retention of a secretion, and in consequence cysts of this description are called *retention* cysts. In other cases it is not clear that the cysts depend upon the retention of a secretion, and yet any other explanation of their origin is difficult. This is the case with cysts that arise in connection with the remnants of the parovarium which represent the fœtal Wolffian ducts, and are normally obliterated (parovarian cysts). Of this kind, too, are probably the cysts met with in the kidney, whether congenital or acquired.

A second variety of cyst is that which surrounds a foreign body which is aseptic. This form of cyst has a wall composed of newly formed but dense fibrous tissue, and its method of formation is identical with the formation of a capsule in the process of encapsulation. That is to say, inflammation plays an essential part in its production.

Closely allied with the method of cyst formation last mentioned are cysts in which the cyst-wall is a part of the foreign body itself. Of this kind are hydatid cysts, cysticerci, &c. They lead to the formation of an additional cyst-wall after the method referred to in the last paragraph, owing to the irritation to which they give rise.

A fourth class of cysts results in consequence of the softening of some previously solid substance. As a rule this depends upon some degenerative process, and we meet with this kind of cyst as a complication of the solid tumours. In a number of cases the softening is localised and partial only, and then we may more justly speak of the occurrence of a cystic degeneration of the tumour; but sometimes the cystic change affects the entire growth, and then the term 'cyst' is fairly to be applied. Sarcomata are somewhat liable to a modification of this kind, the entire growth becoming the seat of a myxomatous degeneration, with the exception of the growing margin.

A fifth class of cyst is also sometimes described and comprises the hæmatomata or cysts containing fluid blood. In some cases these hæmatomata are simply soft tumours (usually sarcomata) into which extensive hæmorrhage has taken place, and it is always important to be on one's guard as to this possibility in the case of every hæmorrhagic cyst. But in many cases which come under the surgeon, and in a few which are seen by the physician, the cyst contents are truly blood which has been extravasated as the result of injury to the vessels and which has not coagulated. In these cases the cyst-wall is composed of the ruptured tissues into which a certain amount of the effused blood has penetrated and has coagulated.

It is often easy to decide to which of these classes a given case properly belongs, but in other instances it is difficult or impossible. Thus in the case of the thyroid body we meet with a cystic condition in which there is a large amount of colloid in the cysts. Here we may have to do in some measure with a definite retention, but in some measure the condition is a degeneration, or rather an excess of a degenerative process which is normal. Of course in this, which is a ductless gland, the ducts, so far as our present standpoint is concerned, are represented by the alveoli themselves.

The last example brings us to the fact that the contents of cysts are determined by the tissue in which they arise. Thus cysts in connection with the sebaceous glands contain sebaceous material, those arising from mucous glands contain a fluid which consists of a large part of mucin, and in the breast we meet occasionally with galactoceles in which the contents are more or less altered milk. But this rule is not without exceptions. Although a cyst of the thyroid body frequently contains colloid material, it is not uncommon to meet with thyroid cysts having fluid contents in which there is no trace of colloid. So, too, the cysts one finds in the kidney when that organ is the seat of ‘ cystic degeneration ’ frequently contain a small amount of urea, but in their other characters the contents can hardly be termed urine ; and in the case of the cysts that are not congenital but acquired, the cystic contents have no further resemblance to urine than their fluidity and their colour, and neither of these is constantly one and the same.

If hæmorrhage takes place into a cyst, the colour of the cystic contents is naturally changed. Frequently the hæmorrhage has taken place at some far-distant time, and then the contents of the cyst are amber, orange, or yellow in colour, corresponding to the formation of some one or other of the pigments produced in the disintegration of blood.

(*b*) **Cystomata.**—It is not uncommon for the cysts to be collectively spoken of under the name ‘ cystomata,’ but it is better to reserve this term for such cystic formations as lead to the production of definite tumours. In some cases the term is still further modified owing to the fact that the histological characters of the solid portions of the cystic tumour are composed of adenomatous tissue. Under these circumstances we have the growths known as cystadenomata.

Whereas it is the rule that the cysts, and particularly the retention cysts, are unilocular, it is far more common for the cystomata to be multilocular. This is well seen in the case of cystomata formed in the ovary. In this organ it is common to meet with cystic growths which may be so small that they are almost microscopic, or may be so large that they occupy the entire abdomen. In either case they are multilocular, in this respect forming a great contrast to the cysts of the parovarium, which are always unilocular, though they may rival the others in size.

In a sense all the cystomata may be said to be cystadenomata. That is, there is always a definite epithelial lining to their walls, and we must suppose that the cystic contents are formed by the functional activity of the cells composing this epithelial lining. In many cases the epithelial cells are not of a very definite form, so that it is difficult to decide the class of epithelium under which they should be placed. True cuboidal or spheroidal epithelium is very rarely met with; in the majority of cases the cells have a more or less close resemblance to columnar epithelium. Sometimes the cells are typically columnar in shape, and this is generally the case with cystadenomata of the kidney, certain varieties of cystoma of the ovary, and similar growths of the testis. On the other hand, a large number of the cystomata of the ovary show a lining membrane composed of cells which are distinctly flattened and which, instead of possessing an elongated or oval nucleus, have one which is round. The same is true of some of the cystadenomata of the thyroid. It is difficult to say whether this appearance of the cells is the result of the pressure

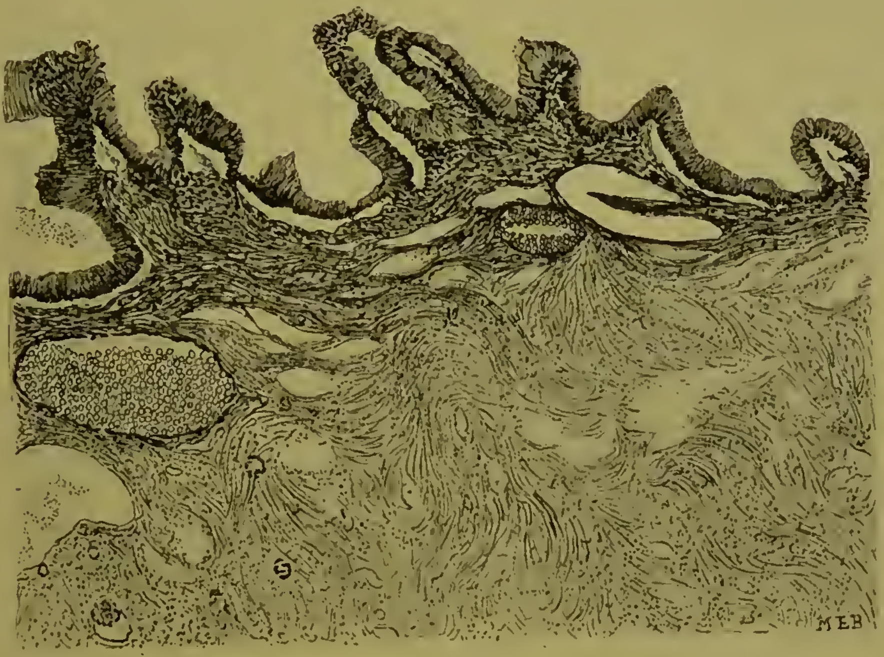


Fig. 59.—Section of Wall of Papilliferous Ovarian Cyst. × 80.

The wall of the cyst consists of fibrous tissue carrying blood-vessels. Internally it is lined by a single layer of columnar epithelium, and at places fibrous tissue and epithelium are prolonged into processes. The upper margin of the figure is therefore the *internal* surface of the portion of cyst-wall.

of the accumulated secretion, and is therefore, so to speak, artificial, or whether the fundamental shape of the cells has become altered during the process of formation of the tumour. In cases in which the cells composing the lining membrane of cystomata are definitely columnar, it is common for 'goblet cells' to be present. These cells may exist in very large numbers, and it is to them that we must ascribe a large proportion of the mucin and paramucin that is contained in so many cystomata.

A considerable number of the cystadenomata are relatively simple in their composition. They consist of a number of round or oval spaces (in section), which are lined by a regular layer of somewhat flattened epithelium, and which contain evidences of the material that originally lay within them. The spaces vary considerably in size, even in the more solid portions of the tumour, and when we consider that the cysts themselves, which constitute the characteristic feature of the tumour, are nothing more than large examples of the same condition, it is clear that the limits are exceedingly wide. It is nothing uncommon, in the case of a multilocular ovarian cystoma, to meet with individual cysts measuring six inches in diameter.

Irregularity in shape of the spaces in the cystadenomata is far less common than it is in the case of the adenomata that are not cystic. The reason of this is not far to seek, for the contents of the cysts are either liquid or at most semi-solid, and therefore the pressure that they exert upon the wall which confines them is manifested in all directions equally. As a result the cross-section of the spaces in the cystadenomata is approximately a circle. Some degree of exception must however be made in the case of the proliferating or papillomatous cystadenomata, to which reference has already been made under the name of villous columnar carcinomata (p. 217).

Besides the substances which are found in cysts and may be regarded as the definite products of the activity of the cells lining their walls, and besides blood and its derivatives, to both of which reference has already been made, we not infrequently meet with crystals of cholesterin. These crystals are principally found in cysts which have been in existence for a long time, and we must probably regard them as indicative of degeneration. There is little doubt that they are formed by, or at the expense of, the epithelial cells, and it is therefore in cases of cysts and cystic tumours which are lined by an epithelium that we meet with this substance. Its occurrence is otherwise not confined to any one variety of cyst or cystoma, though it is commoner in some situations than in others. Thus it is very frequently found in ovarian cystomata, but it may be present in the contents of a hydrocele, or the fluid resulting from the degeneration of a solid tumour such as a sarcoma of the kidney. In the latter instance, although the growth itself is not epithelial, it must be remembered that in the growth of the tumour a considerable portion of the renal epithelium undergoes degeneration.

The solid material which lies between the individual cysts is, in the case of most cystomata, simple connective tissue, but in cases in which the cystic condition is rather a special modification of an original tumour this is not necessarily the case. In cystic sarcomata, for example, the substance between the cysts consists of sarcoma cells. A more important difference obtains in the case of some of the tumours of the testis. Here we meet with connective tissue as the principal element of the inter-cystic material, but a certain amount of muscle and sometimes of cartilage is often present in addition.

TERATOMATA OR DERMOID CYSTS

Although the teratomata are characterised by the formation of cavities contained by a wall, and although these cavities are filled with material which is in the majority of cases of semi-solid consistency, it is better to separate them from the cysts and the cystomata because of their different mode of origin.

Teratomata are of two different kinds. The one kind, it is generally held, results from the inclusion of a portion of the epidermis during intra-uterine life when there is a closure of two approximating processes of epidermis, the other kind is regarded as representing an impregnated but blighted ovum. Corresponding to the different origins that are ascribed to the two kinds of teratoma, the seats at which they are found differ also. Those which arise from an epidermal inclusion are found in situations at which such closure of apposing layers of epidermis occurs. Thus they are met with in the neck along the lines corresponding to the branchial clefts, at the base of the brain, in the orbit, &c. The teratomata which are regarded as arising in blighted ova, on the other hand, are found chiefly in the ovary. They may, however, occur anywhere in the body owing to inclusion of such a blighted ovum within the tissues of a normal twin fœtus.

Ovarian dermoids constitute the great majority of teratomatous tumours, and at the same time they are often more complicated in their structure. The cutaneous dermoid has a wall which is built up of epidermal structures. Hence we find a well-marked squamous epithelium with hair sacs, sebaceous glands, and sweat glands. In ovarian dermoids, in addition to these elements, it is not uncommon to find elements belonging to other systems of tissue, such as bone, cartilage, and even muscle and nerve. Teeth, too, epidermal structures which are not found in cutaneous dermoids, are found with fair frequency in ovarian dermoids. Sometimes they are set in a piece of bone which has a resemblance to a jaw, but far more commonly they are simply inserted in the wall of the cyst. They resemble more closely the milk teeth than the permanent, but as a matter of fact they do not correspond to any normal type. Definite fatty tissue is also found at times, and occasionally the fat may constitute what may fairly be termed a lipoma.

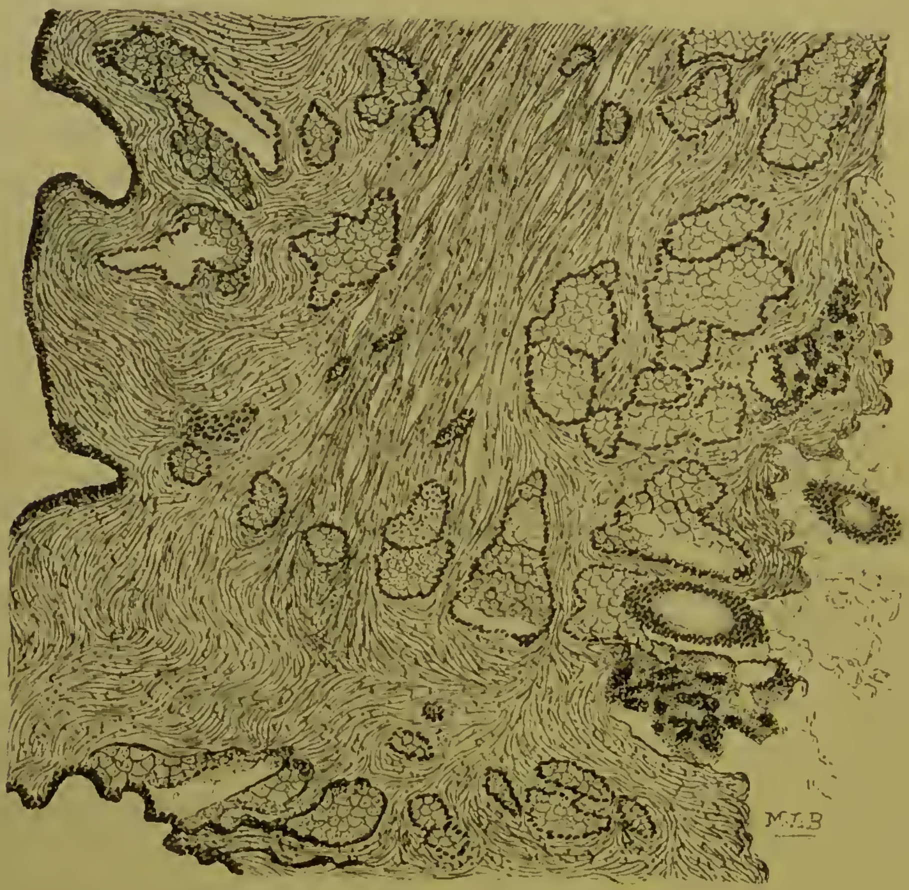


FIG. 60.—SECTION OF WALL OF DERMOID CYST. × 60.

Internal surface of cyst-wall (left), covered with epidermal layers. The wall itself consists of fibrous tissue carrying numerous irregular sebaceous glands and (right) two hairs cut obliquely, two sweat glands, and fatty tissue.

In all dermoid cysts the wall consists principally of a squamous epithelium composed of numerous layers, shows well-marked papillæ, and holds numbers of hair follicles and sebaceous glands. The hair follicles may or may not be numerous, but the sebaceous glands are usually developed to an excessive extent. Both hair follicles and sebaceous glands are functional, too, so that the contents of a dermoid cyst are characterised by the presence of hairs among the greasy material which forms the chief content of the cyst and which is produced by the sebaceous glands.

By some authors certain of the cysts met with in the testis, parotid, and kidney are included among the teratomata, although they cannot be classed among the dermoid cysts. Such of these growths as are definitely congenital, and consist of tissues which have been set apart during intra-uterine life (e.g. rhabdomyoma of the kidney), may perhaps be thus described, but it does not appear advisable to separate them from their natural position among the true tumours, and force them into an unnatural position alongside formations which are so widely different as the dermoid cysts.

Closely allied to the cutaneous dermoids are those formations which definitely depend upon implantation of epidermis during extra-uterine life. These formations are spoken of as **implantation cysts**, and they are formed when some portion of the epidermis has become included in the deeper tissues during the healing of a wound. As a rule, any epidermis which is thus included undergoes atrophy, but occasionally it continues to grow, with the result that a cyst is formed. These cysts are rarely of any considerable size; their walls are formed of squamous epithelium which carries the structures peculiar to the system. As might be expected, implantation cysts are most commonly met with upon the hands. They are also met with in the neighbourhood of a cicatrix, but this fact may not be easy to make out, either because a long time has elapsed since the original injury, or because the injury itself was of slight extent.

PART II

THE PATHOLOGICAL ANATOMY AND HISTOLOGY OF SPECIAL ORGANS AND TISSUES

SECTION I

THE PATHOLOGICAL HISTOLOGY OF THE BLOOD

The pathological histology of the blood resolves itself into a consideration of the different changes which are undergone by the corpuscular elements and the blood platelets. No doubt changes in these directions do not constitute the whole, or even the principal part, of the changes which the blood, considered as a complex tissue, undergoes. But since we are unable for the most part to correlate changes concerning the plasma with any histological appearances in that fluid, consideration of the plasma will not come under our notice. The case is different when the plasma or a portion of it has escaped beyond the confines of the vessels either in inflammatory or in other forms of œdema, but these states have been, or will be, considered in their proper places.

THE RED CORPUSCLES

Although numerically the most important element of the blood, the red corpuscles do not undergo any great range of morbid alteration. They may be present in too small numbers, or may be particularly prone to degenerative changes; they may contain too small an amount of hæmoglobin, or they may enclose parasites, but these are practically the only alterations that we meet with in the red corpuscles in disease.

It is very necessary, in attempting to form an opinion as to whether the blood corpuscles are normal or not, to have a good acquaintance with the various alterations which take place in the blood as the result of agents employed in the preparation of blood films, whether dried, fixed, and stained or examined directly. This is not the place to enter into a description of the manifold errors that may arise from an insufficient knowledge upon these matters. But it may be freely stated, without chance of contradiction, that by far the greater number of abnormal appearances yielded by the red blood corpuscles are pure artefacts, even if we disregard all changes of a gross kind, in which the effects of chemical or physical agents are manifest.

(*a*) **Oligocythæmia.**—The condition of the blood in which the number of red corpuscles is below that which is considered to be normal (5,000,000 per cubic millimetre in the adult male, and 4,500,000 in the female), is known as **oligocythæmia.** But under this name it is generally tacitly implied that no other morbid condition of the blood obtains beyond the deficiency in number of the red corpuscles.

In its purest form oligocythæmia may be seen in cases in which there has been a moderate loss of blood as the result of hæmorrhage. The number of red corpuscles (erythrocytes) may be then as low as 3,000,000 per cmm., but more commonly the fall is not so considerable, or if the hæmorrhage has been sufficiently severe to lead to so pronounced an oligocythæmia, other factors supervene and alter somewhat the morbid appearances of the blood.

In pure oligocythæmia the erythrocytes that remain within the vessels are not conspicuously altered from the normal. It may be possible to recognise that the individual cells are not quite so definitely biconcave as normally, but on the contrary show some tendency to biconvexity. This is due to the lowering in specific gravity of the blood plasma which follows upon a somewhat severe hæmorrhage, and the absorption by the corpuscles of an additional amount of water. At the same time a certain amount of the hæmoglobin may leave the corpuscles, with the result that the blood plasma becomes more or less deeply tinged with red.

Apart from conditions of this kind, a large number of diseases are accompanied by an oligocythæmia. But here the condition is not uncomplicated. It is usually conjoined with a deficiency in the amount of hæmoglobin in the individual corpuscles, and is often further complicated by the presence of signs of blood regeneration, as well as by evidences of degeneration of the red corpuscles.

(*b*) **Oligochromæmia.**—It is an undoubted fact that in certain conditions the amount of the hæmoglobin in the corpuscles is less than normal, though it is uncertain whether oligochromæmia is as common a condition as is usually supposed.

In the majority of cases it is impossible for us to recognise any difference in the corpuscles under the microscope, so far as the amount of pigmentary substance which they contain is concerned. We can only arrive at an estimation by examining them in bulk. This may be done directly, by determining the hæmoglobin value of a definite mass of the corpuscles obtained after centrifugalising the blood, or indirectly, by estimating the hæmoglobin value of a definite volume of blood and correcting the integer thus obtained by the percentage of corpuscles present, as compared with the number present in normal blood. The latter method is the one usually adopted, and by it we may find that the hæmoglobin value of the individual corpuscles is half the normal or even less.

As a rule oligochromæmia occurs along with oligocythæmia. Such is the case in most examples of the anæmia which affects young women (chlorosis), but even in chlorosis we may meet with cases in which the anæmic condition is due to a pure uncomplicated oligochromæmia. In other morbid states the same deficiency in numbers and in the amount of hæmoglobin present in each corpuscle is the characteristic modification of the blood. But in the disease known as **pernicious anæmia**, although the actual number of red corpuscles is enormously diminished—and *a fortiori* the hæmoglobin value of the *blood* also—the hæmoglobin value of the individual corpuscles is not diminished, and, indeed, may be above the normal.

(*c*) **Erythrocytes of abnormal sizes.**—Although it is true that the red corpuscles in normal blood are not absolutely equal in diameter in all cases, even in a given specimen of blood, the differences are so small that it is necessary to measure the individual cells with a micrometer in order to convince oneself of the fact. But in the various morbid states of the blood variations are very common, especially in the severer forms of blood disease.

The diameter of the normal erythrocyte is approximately $7 \cdot 5\mu$, and corpuscles smaller than these are termed **microcytes**, while those of larger size are called **megalocytes**. In normal blood microcytes and megalocytes together account for about 14 per cent. of the total number of red corpuscles, but in pathological blood the microcytes and megalocytes may be far more numerous. Indeed, they may equal in numbers the corpuscles of normal diameter, so that it becomes impossible to say with certainty what is the form of cell present in largest numbers. Between the limits that have been given there is the widest variation, so that the microcyte is not a cell with a fixed diameter, but is only one less in size than the normal. Thus in these severe forms of blood disease the red corpuscles may vary between about $2{\cdot}5\mu$ and perhaps 10μ.

(*d*) **Poikilocytosis.**—In conditions in which we meet with large numbers of microcytes and megalocytes, it is common to find red corpuscles that are very irregular in shape. The commonest form is one which resembles a pear, but more than one prolongation may be present, and often it cannot be said that the corpuscle has a particular shape. This condition is known as **poikilocytosis.**

Poikilocytosis, as such, is not necessarily a sign of an abnormal condition of the blood corpuscles, for it is not infrequently observed at some points of a blood film which at other points clearly shows that the erythrocytes are perfectly normal. In these cases we must conclude that the appearance is due to the method of preparation.

We are still ignorant as to the actual method whereby poikilocytosis is produced. It is, however, practically certain that we must regard the phenomenon as a sign that the corpuscles are more than ordinarily labile, and we have further evidence of this in the fact that blood in which the erythrocytes show poikilocytosis is very liable to 'lake,' i.e. there is a greater tendency than normal for the hæmoglobin to leave the corpuscles. In any case we may take it as certain that a patient whose blood exhibits poikilocytosis is suffering from a very severe illness, whether that illness is one primarily involving the blood and the hæmatopoietic tissues or not.

(*e*) **Nucleated red blood corpuscles.**—It is very unusual to meet with nucleated red corpuscles in the normal blood, and in the various morbid blood states it is not very common. For the presence of nucleated red corpuscles implies that the blood-forming tissues are carrying out their function with so much rapidity that incompletely formed corpuscles are introduced into the circulation. From this it also follows that the nucleated cells are most liable to be present in cases of anæmia which suddenly supervene (e.g. hæmorrhage) in otherwise healthy persons. It is always to be regarded as a sign of blood regeneration.

It must not be supposed from what has been said in the preceding paragraph that nucleated erythrocytes are absent from the blood of cases suffering from the severer and most intractable varieties of anæmia. Such is not necessarily the case, though it is often the fact. Even in the very worst cases we may meet with these cells to the end, but they are generally present in very small numbers.

The nucleated red corpuscles which have hitherto been referred to are of about the same size as the normal erythrocyte, and for this reason they have been termed **normoblasts**. In addition to these cells we also meet with cells corresponding to the megalocytes, and therefore called **megaloblasts**. Microblasts are not known to exist, and this is an important reason for considering the microcyte, not as an independent variety of red cell, but a result of the disintegration of a normal erythrocyte.

When it was said above that the nucleated red cell must be regarded as a sign of blood regeneration, this must not be regarded as a satisfactory sign, unless the nucleated cells are normoblasts. The megalocyte is an abnormal element of the blood, and the megaloblast is even more abnormal. It indicates not only that the blood-forming tissues are being called upon strenuously to repair an antecedent loss of red corpuscles, but also that they are themselves in an abnormal condition, and are unable to turn out properly formed erythrocytes. The presence of megaloblasts in the blood is therefore an indication of the gravest significance.

It is not necessary to describe the nucleated varieties of red corpuscles at any length. For they are relatively simple cells, and consist of a protoplasm which stains with acid dyes such as eosin, show a yellowish colour when unstained from the presence of hæmoglobin, and contain a relatively large round nucleus that stains deeply with basic dyes such as methylene blue.

(*f*) **Other degenerated forms of erythrocytes.**—We have placed the poikilocyte by itself, inasmuch as it is the commonest form in which we meet with degeneration in the case of the red cell, and the view that microcytes are but degeneration products of the same cells has been mentioned. In addition to these, we sometimes meet with red corpuscles which have undergone a form of necrobiosis that was first described by Maragliano, and is therefore spoken of as Maragliano's degeneration. In it the red cells lose their selective power of staining. Thus, they fail to take up the eosin in a mixture of eosin and methylene blue, but on the contrary refuse to stain at all. This peculiarity first shows itself in the centre of the corpuscle, but ultimately it involves the entire cell. According to Maragliano cells which show this peculiarity also are apt to manifest amœboid movements. Ultimately they become poikilocytes.

Another form of degenerated red corpuscle is represented merely by the outline, so that they may be described as 'ghosts' (German, 'Schatten'). Whether these forms are but extreme examples of Maragliano's degeneration it is impossible to say; indeed it is doubtful whether both forms of degeneration are not purely artificial in their origin.

Another and undoubted result of the degeneration of red corpuscles consists in the presence of granules of pigment derived from the hæmoglobin. The best example of this change is seen in malaria. In this disease, as we shall see later, the parasite destroys the erythrocyte, with the production of granules of pigment which it takes up into itself and bears within its body for a considerable length of time. Pigment granules may also be found circulating in the blood plasma in very severe cases, but far more commonly they are deposited in the solid organs, particularly the spleen.

Other signs of destruction or degeneration of red cells are to be observed in hæmoglobinuria and in the deposit of particles of iron derived from the hæmoglobin in the liver, kidneys, &c., but these conditions will be considered more conveniently in other places.

THE LEUCOCYTES OR WANDERING CELLS

Before considering the morbid changes of the blood that affect the leucocytes especially, it is necessary to say a few words concerning the varieties of colourless cell met with under normal conditions.

The colourless cells met with in the blood may be divided into two great groups according as they hold granules in their protoplasm or not. A further differentiation is made among the granular cells according as the granules stain with different aniline dyes.

The aniline dyes are chemical substances which enter into combination with one another and with certain other substances in a fashion which has its correlative in the combinations between acids and bases. For this reason the dyes themselves are divided into acid and basic, eosin being an example of the acid class and methylene blue an example of the basic class. Neutral dyes are also known; in their composition they correspond to salts, but they do not enter largely into histological considerations of the blood.

The granules of the granular leucocytes show a selective reaction to these stains, so that in a mixture of eosin and methylene blue some granules will take on a red colour, while others will be stained blue or purple.

The granules in a given cell almost always are of one kind, so that the cells themselves have been divided into *acidophil* or *oxyphil* and *basophil*. Moreover the size of the granules differs, so that we are able to distinguish between cells with large granules and those with small.

Besides a difference in the chemical and physical natures of their granules, the granular leucocytes show differences in their sizes and especially in the shapes of their nuclei. To the full description of these cells we shall return shortly.

The non-granular leucocytes differ from one another principally in their size and in the characters of their nuclei. As we shall see later, however, they differ in the more important matter of their functions.

If we omit from consideration cells which are but rarely found and may then be regarded, so to speak, as accidental, the leucocytes found in normal blood are of the four following kinds—(*a*) cells with fine oxyphil granules, (*b*) cells with coarse oxyphil granules, (*c*) large cells without granules termed *hyaline* cells, and (*d*) non-granular cells of small size termed *lymphocytes*. These cells will first be described, and afterwards mention will be made of those colourless cells which are found in the blood under pathological conditions.

(*a*) **Finely granular oxyphil cells.**—These cells are the commonest of all the hæmal leucocytes, forming 60–70 per cent. of the entire mass of leucocytes met with in normal blood. They do not differ greatly from one another in size, and measure, on an average, 8–9μ. They have a very irregular nucleus which stains deeply with all nuclear dyes. These nuclei are quite characteristic of the variety of cell; sometimes they appear to be multiple, but more commonly they are multilobed, or convoluted, or sinuous. The oxyphil granules show a considerable amount of variation in their appearance. Sometimes they are very distinct, but sometimes they are packed so closely together that, when stained, they give to the protoplasm of the cell a uniform red appearance. In such cases it is difficult to say that we have to do with a granular cell, and it is only from the characters of the nuclei that we are certain. It is, of course, possible that in such instances we have not in reality to do with actual granules, but that the protoplasm of the cell contains an undifferentiated material which stains with acid dyes, is analogous with the granules, and perhaps is an antecedent of the granules. But upon this point it is impossible to dogmatise.

The number of oxyphil granules in the cells varies widely. In some cells we may find that the protoplasm is, at first sight, colourless, and only after careful examination are able to find a few minute granules which are stained a light pink colour. In other cases the cells form very beautiful microscopic objects, the granules being numerous, stained a bright rose-pink, and contrasting well with the deep blue and tortuous nucleus. As a rule, one or other variety of staining affects the whole of the cells in a given blood film.

It is necessary to mention that the finely granular oxyphil cell is also known by other names. From the character of its nucleus it is often termed 'polynuclear,' or more accurately 'polymorphnuclear.' On the Continent it is frequently spoken of as the 'neutrophil' leucocyte. This name was given under a misconception, but is still often employed.

(*b*) **Coarsely granular oxyphil cells.**—These cells are somewhat larger than the finely granular variety, measuring, on an average, 10-11μ in diameter. The granules with which their protoplasm is packed are larger than in the finely granular cells, and take on the acid dyes with more avidity, so that a blood film which has been insufficiently stained with eosin to colour the granules in the finely granular cells, may nevertheless show the coarse granules quite clearly. Owing to their larger size and also to their intense refractive power, the coarse granules form conspicuous objects when viewed in mass. Their bright rose-red colour allows the cells in which they are present to be easily distinguished with the low powers of the microscope.

The nucleus of a coarsely granular oxyphil cell in its typical form is that of a horseshoe, but it is not always easy to see that this is the case. In any case the nucleus is quite different from that of a finely granular oxyphil cell, not only in its shape, but also in the point that it stains far less deeply. Sometimes it appears as if the cell had two nuclei, but more than two are rarely seen. Even when two nuclei are apparently present, they are both round and of the same size, so that it is possible that they are really the ends of the horseshoe seen from above.

This variety of cell, owing to its characteristic staining in a mixture of eosin and methylene blue, has been called the 'eosinophil cell,' and when this expression is used in literature it is to the coarsely granular oxyphil cell that reference is made.

In some of the lower animals, and sometimes also in man, the granules seem to be held less firmly within the protoplasm of the cell than is normally the case. As a result when blood films are made, the granules are found lying all round the disintegrated cell, and free. These cells have been described as 'explosive cells,' but it is not certain that they differ otherwise from the cell described above as the normal one.

In the normal blood of man, the coarsely granular oxyphil cells constitute 2 to 5 per cent. of the total number of leucocytes. In many of the lower animals there does not appear to be a distinction between cells with large and small oxyphil granules. In the frog, for example, the only oxyphil cells found possess coarse granules. And sometimes in man, when the fine granules are especially conspicuous, it is difficult to decide whether the cells under observation belong to the class with coarse granules or to those with fine. It must not be concluded from this that there is a direct relationship between the two varieties, for this is extremely doubtful. To mention only one objection, the finely granular oxyphil cells are intensely phagocytic, the coarsely granular are non-phagocytic.

(*c*) **Hyaline cells.**—These cells differ very considerably in appearance from those which we have just discussed, owing to the fact that their protoplasm contains no granules of any sort. The cells themselves vary much in size, but in a majority of cases they are distinctly larger than any other variety of leucocyte. A good example will measure about 12μ in diameter. The nucleus is either round or oval, is large, and relatively poor in chromatin, so that it stains poorly with methylene blue. It is set in a large amount of protoplasm, which stains very faintly indeed with methylene blue. The outline of the cell is somewhat less regular than the outline of the granular cells. These latter are usually fairly circular, but the hyaline cell frequently has an irregular outline, which, although not actually angular, approaches somewhat towards that type.

By reason of the definite characters of their nuclei, and their contrast to the nuclei of the granular cells, it is not uncommon to give the name 'mononuclear cells' to the class. There is no valid objection to the name, excepting that it etymologically includes the lymphocytes. The typical lymphocyte, however, differs totally from the typical hyaline cell not only in its histological characters, but also in the fact that the hyaline cell is highly phagocytic, whereas the lymphocyte is non-phagocytic.

(*d*) **Lymphocytes.**—These cells are characterised by their deeply staining round nuclei, and their small amount of protoplasm, which, in addition, is non-granular. They are the smallest of all varieties of leucocyte, and show but little variation in their characters. They have the characters of the cells contained in lymphatic glands, from which they are washed into the blood by way of the lymph stream.

It is impossible to state the numbers of hyaline cells and lymphocytes that are present in normal blood, separately. Together they account for 30 to 40 per cent. of the total number of leucocytes, and when one variety is present in large numbers there is a correspondingly small number of the other variety. It may be said, however, that shortly after a meal the number of lymphocytes in the blood is increased.

The cells described above are always to be found in the normal blood, and the total number of leucocytes per cubic millimetre is, roughly speaking, 8,000. During digestion, 12,000 is nearer the mark.

Under pathological conditions the cells that are met with in the blood, in addition to those which have already been described, may be reinforced, or partly replaced, by cells of different characters. These cells are as follows.

(*e*) **Basophil cells with coarse granules.**—These cells are of fairly large size, have a round or oval nucleus which stains faintly with methylene blue, and granules which stain a reddish or bluish purple with the same dye. The granules are not so large as those in the coarsely granular oxyphil cell, but are larger than those of the finely granular oxyphil cell. They are not distributed throughout the protoplasm of the cell with any regularity, nor are they always of one size. These cells are similar to large cells which are to be found in the connective tissue of most vertebrates, and in Germany they are often spoken of as 'Mastzellen.'

(*f*) **Basophil cells with fine granules.**—These cells are about the size of a red blood corpuscle or a lymphocyte. They have a round or perhaps lobed nucleus which nearly fills the cell, and the small amount of protoplasm which is left is filled with small granules, staining a deep purple with methylene blue. The nucleus of the cell takes the stain feebly, so that, apart from the granules, the cell bears considerable resemblances to a small hyaline cell. Moreover, since the granules in this variety do not offer any conceivable difference in size from those in the coarsely granular basophil cell, some authors form one class of the two varieties. Whether this is justifiable is a matter of opinion, but it must be conceded that when one finds basophil cells in the

PLATE VI

Fig. A.—Three coarsely granular oxyphil ('eosinophil') cells (above) and five hyaline cells of the blood (below).

Fig. B.—Finely granular oxyphil ('polymorphnuclear' or 'polynuclear') cells of the blood (above) and lymphocytes (below).

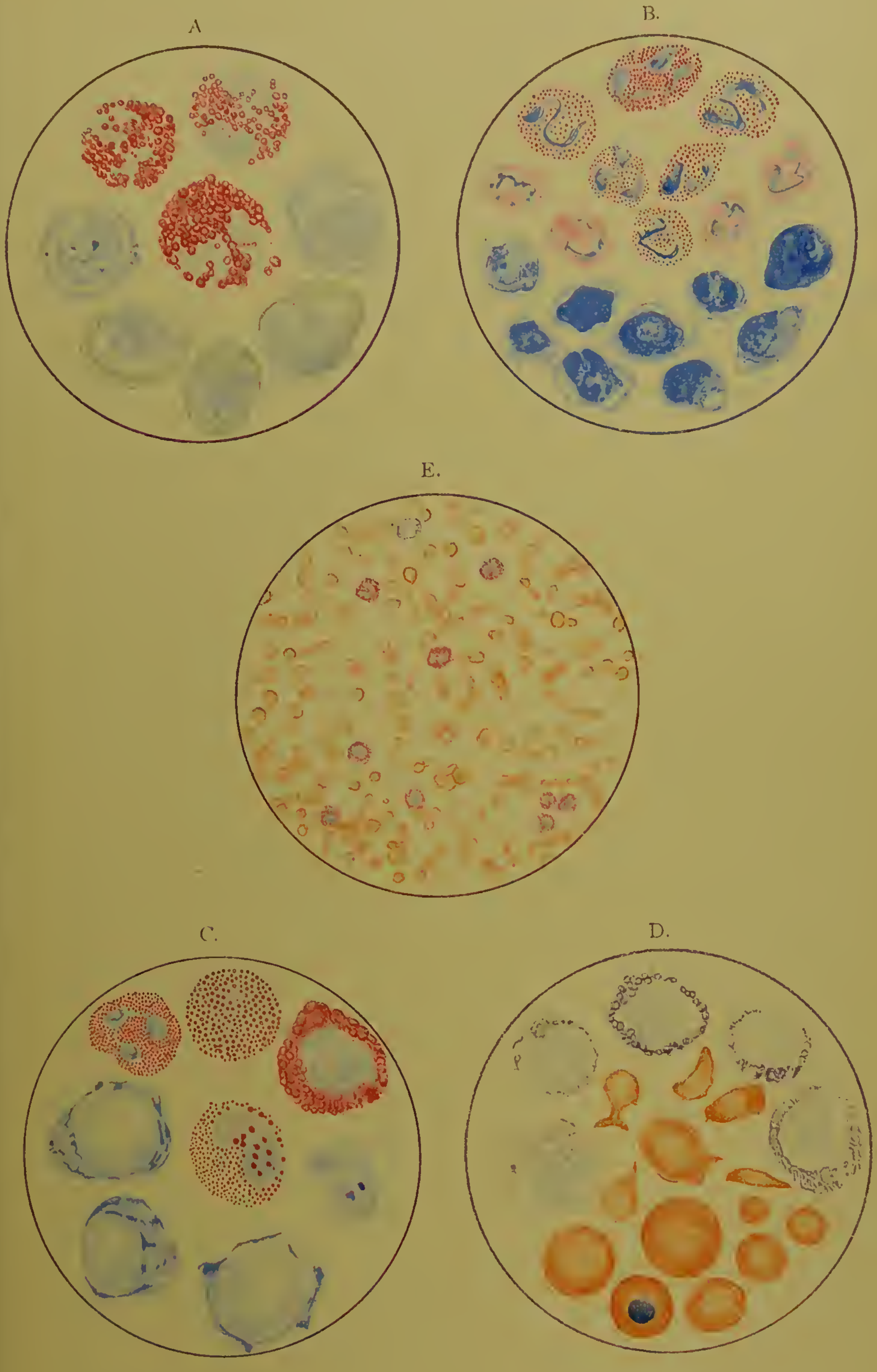
Fig. C.—Atypical leucocytes from a case of spleno-myelogenous leuchæmia (leucocythæmia). In the middle and immediately above are two cells that would usually be termed myelocytes. To the left and above is an atypical finely granular oxyphil cell, to the right and above is an atypical 'eosinophil' cell. The atypical hyaline cells are larger than the normal hyaline cell, and their nucleus generally stains even more faintly than the cell protoplasm.

Fig. D.—Basophil cells (above) and varieties of red blood corpuscles (below). Most of the basophil cells show small granules of a purple colour, but in the topmost cell the granules are large ('mast cell'). In the lower part of the figure to the right of the nucleated red blood corpuscle is represented a normal erythrocyte for comparison. Immediately above are two megalocytes (towards the left) and three microcytes (towards the right). The centre of the figure is occupied by various forms of poikilocyte.

Fig. E.—Coverslip film of blood from a case showing post-hæmorrhagic leucocytosis. Seven finely granular oxyphil cells, two coarsely granular oxyphil cells, one hyaline cell, and one nucleated red blood corpuscle are recognisable.

In all cases the specimens from which the cells represented in the plate were drawn were films fixed by heat, stained by watery eosin and subsequently by watery methylene blue, and mounted in Canada balsam. Figs. A, B, C, and D are magnified 800 diameters, fig. E is magnified 200 diameters.

Plate VI



Varieties of Blood Corpuscles.

blood, one always finds a number of them which it is extremely difficult to refer to one class in preference to the other.

(*g*) **Atypical oxyphil cells (myelocytes).**—Under certain conditions we meet with cells in the blood which bear resemblances to the normal coarsely granular oxyphil cell.

Thus the atypical oxyphil cell is, as a rule, larger than either the finely granular or the coarsely granular oxyphil cell, but it is far more variable in size than those cells. In addition to the difference between its nucleus, which is round, and the nuclei of the normal oxyphil cells, there is a difference in the character of the granules themselves. As a rule they seem to lie, in size, between the coarse and the fine. At the same time they resemble the coarse granules in the fact that they take up the acid stain with great avidity, so that the granules are of a brilliant colour.

(*h*) **Atypical hyaline cells (myelocytes).**—The atypical hyaline cells also differ from normal hyaline cells of the blood, but the difference is less obvious than in the case of the other variety of myelocyte, owing to the absence of granules. Nevertheless the cells are usually of large, albeit of very variable, size, and the magnitude of the faintly staining nuclei compared with the amount of protoplasm makes it difficult to mistake them for any other variety of cell.

The cells that have been described above may therefore be collected into the following table.

	Granular cells		Non-granular cells
Normal . . .	Oxyphil	Fine granules	Hyaline
		Coarse granules	Lymphocytes
Pathological . .	Basophil[1]	Fine granules	
		Coarse granules	
	Atypical oxyphil (Myelocytes)		Atypical hyaline (Myelocytes)

Owing to the fact that the blood is the great highway of the body, not only do a considerable number of morbid processes in the solid tissues lead to changes in the blood, but also, when conditions exist which we are accustomed to regard as diseases particularly affecting the blood itself, the hæmal changes are accompanied by changes in the hæmatopoietic tissues. It, therefore, becomes at times difficult to decide whether a given condition should be discussed under the one heading or the other. On the whole, it is preferable to consider the conditions along with the blood, and this course will be taken here.

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[1] It is not quite accurate to say that the basophil cells are entirely pathological appearances in the blood, for they may be present in normal blood to a very slight extent, as a rule not constituting more than about 5 per cent. of the total number of leucocytes. Sometimes, too, they are found in the blood of persons that we have no reason to believe are other than quite healthy. In these cases they are not of constant occurrence, but are met with now and then, and under circumstances of which we are quite ignorant. The atypical varieties of cells are certainly pathological.

Leucocytosis.—Perhaps the commonest of all pathological conditions of the blood is one in which there is an increase in the number of leucocytes present. This increase may be so slight that it almost comes within the limits of physiological variation, but it may also be so considerable that, instead of the normal 8,000 per cubic millimetre, there may be present as many as 40,000. When a greater number of leucocytes than this is present, we generally have to do with a condition which is more severe than is indicated by the name leucocytosis.

Leucocytosis may be induced experimentally by the most diverse means, and clinically it is met with under a great number of conditions. As a rule, however, it is indicative of the existence within the body of a focus of inflammation, and often of suppuration. This is not *always* the case, for, as has been said when dealing with the subject of inflammation, the degree of virulence of the irritant has much to do with the presence or absence at the focus of irritation of a number of leucocytes, and the same is true of the blood. Hence among the acute infective disorders we find that a favourable case of pneumonia will be accompanied by a good leucocytosis, reaching, perhaps, to 25,000 per cmm., whereas a case that is going to end fatally will very likely show no evidence of leucocytosis during the whole course of the illness. In typhoid fever, as in tuberculosis, syphilis, &c., it is uncommon to meet with a leucocytosis unless some complication arises. The reason of this difference between the diseases is difficult to explain.

Leucocytosis also occurs when a body is the seat of a malignant growth, but the leucocytosis is rarely so well marked when the disease is carcinoma as when it is sarcoma. It is difficult to give figures for the two kinds of tumour, but it may roughly be said that, whereas about 10,000 per cmm. is the average in cases of carcinoma, in sarcoma it is about 12,000. Both of these figures are, however, frequently exceeded. In the case of carcinoma the leucocytosis frequently does not appear till a little before death. Removal of a malignant growth exerts a marked effect upon the leucocytosis, the numbers soon falling again to the normal.

Hæmorrhage, especially if severe, is followed by a marked leucocytosis. This fact is observed with great constancy, but its explanation is difficult. We can account for a portion of the increase in number of leucocytes by the increase in the flow of lymph which follows almost immediately upon the hæmorrhage; this must, of necessity, wash a considerable number of leucocytes from the lymph glands into the general circulation. But the increase in lymph flow can hardly account for the entire leucocytosis, as this lasts for several days, whereas the increase in rate of lymph flow is of short duration. Possibly some condition which depends upon the altered composition of the blood after hæmorrhage acts as a stimulus to the spleen, the lymphatic glands, and the bone marrow, tissues which we know to be intimately concerned with formation of leucocytes.

Leucopenia.—The converse condition to leucocytosis—that in which there is a diminution in the number of leucocytes in the blood—is known as **leucopenia**. Concerning this condition we know but little more than the fact that it exists. Reference has already been made to the importance of the point in connection with the prognosis in a case of lobar pneumonia.

An important question, and one which has not yet been satisfactorily answered, is whether leucocytosis and leucopenia are general conditions or whether they are purely peripheral and local. That there is some balancing between the two conditions seems, *a priori*, probable, and it has been shown that in some cases of severe local inflammation, in which, as will be remembered, there is generally a marked accumulation of granular leucocytes at the focus of irritation, there is at the same time a leucopenic condition of the blood itself.

The varieties of leucocyte involved in the constitution of leucocytosis and leucopenia differ in different cases, but it may generally be said that in leucopenia there is a diminution of all varieties proportionately, in leucocytosis the increase is especially likely to consist in an increase in the number of finely granular oxyphil cells. Thus in leucocytosis these cells often constitute 80 to 90 per cent. of the total number of leucocytes. Sometimes, however, the non-granular cells are chiefly accountable for the increase, while in other cases the increase affects all varieties alike, so that the percentage of each variety remains the same as normal.

BLOOD CHANGES IN THE ANÆMIAS

When so considerable an alteration from the normal composition of the blood has occurred that the complexion of the patient changes and becomes pallid, it is customary to speak of the condition as one of anæmia. Such a condition might theoretically depend upon a diminution in the number of the red corpuscles, upon a diminution in the hæmoglobin value of the individual corpuscles, upon an increase in the number of leucocytes, or upon a combination of two or more of these factors. In point of fact, it is commonest for such a combination of factors to be present; anæmias due to uncomplicated oligocythæmia or oligochromæmia being rare, and anæmia due to an uncomplicated increase in the number of the leucocytes being unknown.

There are many ways in which the anæmias are classified. The commonest is into the primary or essential and the secondary or symptomatic anæmias. Upon the whole, it is advisable to classify them as far as possible according to the characters of the blood, for it is clear that at any time an anæmia which is to-day considered as being an essential anæmia may to-morrow be shown to be merely symptomatic. We shall therefore divide them into (1) anæmias in which changes in the colourless cells of the blood are *absent*, and (2) anæmias in which changes in the colourless cells are *present*.

(1) **Anæmias without leucocytic changes.**—It is unnecessary to enter at any length into a description of the histological appearances of the blood in cases where the red corpuscles are alone concerned. In the greater number of them we have to do with the condition known as chlorosis, and then find that there is a moderate diminution in the number of the red cells, together with a greater or less diminution in the hæmoglobin value of the blood, and therefore of the individual corpuscles. In these cases the proportion of plasma to cells seems to be greater than normal, and the plasma itself is often of a lower specific gravity. As a result the corpuscles tend to become more convex in shape than normal.

In pernicious anæmia the changes are also practically confined to the red corpuscles. There is a profound anæmia, so small a number of corpuscles as 123,000 per cmm. having been recorded. This anæmia does not come on at once, but is progressive. Moreover it proceeds to a fatal issue, and in this respect differs from the entire class of the chloroses.

Another point of difference from the other forms of anæmia, of whichever class they may be, is that when the individual corpuscles are considered in respect of their hæmoglobin content, they are almost always found to contain as much hæmoglobin as normal corpuscles, and in many instances they show a higher index than normal. In this case we have therefore to deal with a very severe and intractable form of oligocythæmia, which is, however, uncomplicated by a deficiency in the amount of hæmoglobin in such corpuscles as are present in the blood. Poikilocytosis is common, microcytes and megalocytes are very numerous, but nucleated erythrocytes are present in very few numbers or are absent altogether. The disease is accompanied by changes in the liver, heart, and diaphragm, and frequently the bone marrow; to these reference will be made in the proper places. It is also common to find a considerable amount of urobilin in the urine.

It is not necessary to refer specially to those varieties of anæmia that depend upon actual loss of blood as the result of hæmorrhage. It need only be said that the degree of anæmia varies according to the amount of blood that has been lost, that the anæmia is in all uncomplicated cases, at first a simple oligocythæmia which may subsequently become modified by the presence of an oligochromæmia, and that nucleated red cells are usually numerous after a short time has elapsed. Poikilocytosis may be present in very severe cases. Mention has already been made of the leucocytosis that supervenes.

In certain cases belonging to the class now under consideration the anæmia is due to the presence in the body of an animal parasite. The two most important of these are the parasites of malaria and the Anchylostomum duodenale. Strictly speaking, there is nothing peculiar in the forms of anæmia which are induced by these parasites. That is to say, we find that the changes are fundamentally a diminution in the number of red cells, conjoined, when the case has lasted for a certain length of time, with a certain amount of oligochromæmia.

The anæmia due to the presence of the Anchylostomum duodenale is nothing more than an anæmia due to persistent small hæmorrhages. The parasite is a small worm that inhabits the duodenum of individuals living in certain districts, particularly Egypt and Brazil. It is a nematode worm 6–10 mm. in length which has a head provided with two strong jaws by means of which it attaches itself to the mucous membrane of the duodenum, jejunum, or ileum, and lives on the blood of its host, which it sucks therefrom. After a time it drops off and the small wound continues to bleed. Since several hundreds of these parasites may inhabit the intestinal canal, the hæmorrhage with which their presence is bound up may become so severe that the anæmia produced in this way is one of the most formidable varieties known.

In malaria the anæmia is due to an insufficiency in the number of red corpuscles, but in this disease they are actually destroyed by the parasites. It is generally allowed that at least three different varieties of malaria parasite exist. These are: (1) the parasite of typical quartan ague, (2) that of typical tertian ague, (3) that of æstivo-autumnal fever. Into the differences between these varieties it is impossible to enter here, but it may be said that in the case of all kinds of malarial parasite it is generally agreed that they may occur under three types. These are: (*a*) spherical bodies (plasmodia), (*b*) crescentic bodies, and (*c*) flagellate bodies.

The spheroidal bodies are those most commonly met with in the blood. They are young forms of the parasite and are first to be noticed as inhabiting the red blood corpuscles. They grow at the expense of these corpuscles, and the products of their digestion and the destruction of the red cell are to be recognised in the black pigment granules which are regularly to be found in the older and larger plasmodia.

Not only do the plasmodia live at the expense of the corpuscles, they also increase in numbers within them. For they multiply by endogenous sporulation, and ultimately are set free in the plasma by rupture of the corpuscle itself. The parasite is, therefore, met with in an endoglobular and in an ectoglobular form.

Crescentic forms are much less frequently found. They are larger than the spheroidal forms, and although it cannot be said that the question is settled beyond dispute, it is very probable that they arise from the spheroidal form. They may be met with free in the blood plasma or may be attached to a red corpuscle. They almost invariably show the presence of black pigment granules in their middle third. Crescentic bodies may be observed in the blood of malarial patients even weeks after the spheroidal forms have disappeared.

Flagellate forms are less commonly observed than either of the others, but it is said that they may be found to develop from crescents in blood that has been shed. They are spherical and are provided with one to four flagella. By means of these flagella the organism freely swims about in the fluid of the preparation.

The entire life-history of the organism has not yet been made out, but a large amount of evidence has been accumulated to show that its existence is largely bound up with the presence of stagnant water. Quite recently, too, it has been observed that forms of the parasite are to be found within the bodies of a certain variety of mosquito (Anopheles). It is owing to the bite of infected mosquitoes that man becomes the subject of malaria.

The pigment found in the bodies of the malarial parasites, though derived from the hæmoglobin, is iron-free. It is, as far as is known, identical in composition with the pigment present in the cells of a melanotic sarcoma, and is called by the same name, viz. melanin.

The varieties of anæmia which are due to the action of some poisonous substance, and are grouped together under the name of **toxic** anæmias, also belong to the group in which leucocytic changes are absent for the most part. Such conditions of the blood are found in cases of chronic poisoning by lead and by arsenic, acute poisoning by chlorate of potassium, arseniuretted hydrogen, and experimentally by a large number of substances. In them all there is a definite destruction of red cells, with, in some of them, hæmoglobinuria and jaundice. But no especial modifications of the microscopical appearances of the blood are present to distinguish them from any other severe form of anæmia belonging to the group.

(2) **Anæmias in which changes in the colourless cells are present.**—In this class is contained the condition known as leuchæmia, but it will be convenient if we also make mention at the same time of a condition which has received a number of names, but which is generally known as 'Hodgkin's disease' or pseudo-leuchæmia.

(*a*) **Leuchæmia.**—Two conditions are recognised in which there is a considerable increase in the number of colourless cells in the blood. These differ to a certain extent in their clinical characters, but in the point that they are characterised by a profound anæmia they resemble one another. A further point of resemblance exists in the fact that the anæmia, although it is most conspicuously one which is associated with an increase in the number of leucocytes, is also one in which there is, at all events when the disease has reached a well-defined stage, a notable oligocythæmia and oligochromæmia. Nevertheless, the actual varieties of leucocyte met with in the two forms are different.

The chief clinical difference between the two varieties of leuchæmia lies in the fact that in the one the spleen is markedly the seat of change, whereas in the other this is not the case, but there is a general increase in size of the lymphatic glands of the body. In that variety, too, in which the spleen is affected, there is a tendency for the medulla of the long bones to undergo change. Hence leuchæmia is divided into the **spleno-medullary** and the **lymphatic** varieties.

In spleno-medullary leuchæmia (also called leucocythæmia), the blood changes are very conspicuous. A blood count shows that the number of leucocytes is far greater than normal. In a case of moderate severity we may find 60,000 or 80,000 per cmm., while in an intense form we may find 300,000. In cases in which besides the great increase in the number of leucocytes there is a severe oligocythæmia, the number of leucocytes may actually be greater than that of the erythrocytes, but such a state is very rare.

The colourless cells present in the blood in cases of spleno-medullary leuchæmia are atypical oxyphil and atypical hyaline cells, and basophil cells. A certain proportion of normal cells is also present.

It has already been said that spleno-medullary leuchæmia is accompanied by certain changes in the medulla of the long bones. We know that this tissue is normally of two kinds, red, which is occupied with the formation of red blood corpuscles, and yellow, which is merely fatty. The red marrow is present in the cancellous tissue, the yellow in the cavity of the shaft.

Now whenever there is a need for the regeneration of red blood corpuscles the red marrow becomes more vascular than usual, and in it are to be found large numbers of cells which are known as erythroblasts, and which are practically identical in characters with the nucleated red cells of which we have spoken above In all moderate cases of anæmia, this change in the medulla is the only one seen. But in very advanced anæmias, and therefore especially in pernicious anæmia, the change extends until the entire mass of the yellow marrow has become converted into a substance having much the same appearance as red currant jelly. Under the microscope it is seen that the change has been accompanied by an almost complete disappearance of the fat globules, and a replacement of the tissue by a loose and highly vascular connective tissue. In the meshwork of the tissue are enormous numbers of nucleated cells the protoplasm of which is in most instances tinged with hæmoglobin, but in some is colourless. So far as the cells are concerned which contain hæmoglobin, we have to deal with precursors of the erythrocytes, but the cells are not normoblasts, but on the contrary are cells of the most variable size. In other words, they are megaloblasts of various sizes mixed with a small number of normoblasts. These cells are not only abnormal, they are also thrown into the circulation before they have undergone the changes corresponding to the formation of normal red corpuscles from normoblasts.

The colourless and nucleated cells which are present in the altered red medulla of the long bones in cases of pernicious and other severe anæmia, are cells to which the name **leucoblast** has been given. In pernicious anæmia they are not present in as large numbers as the nucleated precursors of the red cells. Nor is there the same degree of certainty in regard to their relation with the normal leucocytes of the blood. But it is commonly held that they are in the same way somewhat abnormal precursors of the leucocytes, and also are thrown into the circulation before they have undergone all the changes which they undergo in normal life. That this is probably true is shown by the fact that in spleno-medullary leuchæmia the number of leucoblasts in the bone marrow is so considerable that the marrow takes on an appearance somewhat resembling that of pus.

Although there is no doubt that the bone marrow is an important seat of change in cases of extreme anæmia, being perhaps the cause of the hæmal modifications seen in pernicious anæmia owing to an abnormal formation of red cells, and the cause of the abnormal appearances in leuchæmia owing to an abnormal formation of leucoblasts, it must not be supposed that the only changes in leuchæmia are to be met in the bone marrow. Thus in the spleno-medullary form there is a tendency for abnormal forms of leucocyte to be met with in the spleen, and although they might possibly have arrived there after being formed in the bone marrow, it is more consistent with our knowledge of the functions of the spleen to believe that the spleen is the seat of their formation.

Whether the lymphatic glands take a part in the formation of leucocytes in spleno-medullary leuchæmia is doubtful. In any case they are far less important in this variety than they are in lymphatic leuchæmia.

In lymphatic leuchæmia (also known as lymphocythæmia) the anæmia is considerable, though perhaps it is not quite so profound as in the spleno-medullary form. Moreover, the facts that the spleen is not enlarged, or not markedly enlarged, that, on the contrary, there is a considerable and universal enlargement of the lymphatic glands throughout the body, and that the characters of the blood are quite different, afford other points of contrast. So far as the blood is concerned, although there is in lymphatic leuchæmia a very considerable increase in the number of leucocytes, it is not usual for them to be present in such enormous numbers as is sometimes the case in spleno-medullary leuchæmia. The character of cell present, too, differs, for in lymphatic leuchæmia the colourless cell found is always a lymphocyte that can hardly be differentiated from the ordinary lymphocyte, if it is not actually identical. Its presence in the blood is no doubt to be correlated with the increase in size of the lymphatic glands which characterises the disease.

Lymphatic leuchæmia is a decidedly more rare form of the anæmias of Group II. than the spleno-medullary variety. As to the changes of the bone marrow in the condition we are not yet in a position to speak with certainty, but it is, *a priori*, improbable that they will be found to be like those in spleno-medullary anæmia.

(*b*) **Pseudo-leuchæmia, lymphadenoma, or Hodgkin's disease.** In this disease the clinical and pathological characters are somewhat variable, but it may be said that in general there is an enlargement of a number of the lymphatic glands of the body, together with, probably, some enlargement of the spleen, and a modification in the number of leucocytes in the blood.

So far as the lymphatic glands are concerned, an enlargement may be taken as almost characteristic of the disease. This enlargement may affect the whole of the glands of the body, or it may be confined in some degree to one or more systems. Nor are the lymphatic glands alone affected, for the change involves the lymphoid tissue of the body generally. The glands are discrete, a matter of considerable importance to remember, for a condition is known in which the glands tend to become fused at the same time that they are enlarged. This latter condition is known as lympho-sarcoma, and although it is probable that in some cases a lympho-sarcomatous change may develop in the enlarged glands of Hodgkin's disease, such a modification is certainly rare, and in their typical forms the two diseases are distinct.

Considerable difficulty has been introduced into the question now under discussion owing to the fact that the nomenclature of the diseases in which there is an enlargement of the lymphatic glands is very variable. Thus the disease which we are considering under the name of pseudo-leuchæmia is not only termed Hodgkin's disease in this country, but also lymphadenoma, while on the Continent there are authors who speak of it under the name of lympho-sarcoma. On the whole, the name 'pseudo-leuchæmia' is best, for there is no doubt that anæmia of a moderate degree is present with great regularity, that it has many resemblances in its clinical characters with true leuchæmia, and that in a fair number of instances the blood shows the presence of a considerable increase in the number of leucocytes. It is probable, however, that the resemblances are more superficial than real. Some authors, indeed, are inclined to place pseudo-leuchæmia among the chronic inflammatory diseases, and it has even been asserted that lymphadenoma is nothing more than a specialised variety of tuberculosis affecting the lymphatic glands.

The variety of true leuchæmia with which Hodgkin's disease has the most clinical resemblance is certainly that of lymphatic leuchæmia. But, however close the resemblance clinically, an examination of the blood is always sufficient to distinguish between them. For whereas in lymphocythæmia there is always an increase in the number of lymphocytes, in Hodgkin's disease there is sometimes no increase in the number of leucocytes at all, and even in those cases in which there is an increase, the cells which form the increase are not lymphocytes but finely granular oxyphil cells.

It is very difficult to give data as to the modification of the blood present in pseudo-leuchæmia other than that mentioned in the last paragraph. For, although it is the rule that the disease is accompanied by anæmia, there is the greatest variability in the characters of the anæmia. In the majority of well-marked cases it may probably be said there is a diminution in the number of erythrocytes, often accompanied by a moderate diminution in the hæmoglobin value of the individual corpuscles, and that this occurs in conjunction with an increase in the number of leucocytes. In all cases in which the blood shows an increase in the number of leucocytes there is a relative as well as an actual increase in the number of finely granular oxyphil cells.

It is not proposed to enter into a description of the condition which has been termed 'splenic anæmia' or 'splenomegaly,' owing to the fact that little is known concerning it. It is probable, indeed, that more than one condition is included under the name. But it may be mentioned that in one variety of the disease, at all events, there is a progressive increase in the size of the spleen, which may or may not be accompanied by a progressive anæmia. This anæmia is certainly secondary, and too little is known concerning its characters for us to delay over them.

THE BLOOD PLATELETS

Very little is known concerning the modifications of the blood platelets in disease, and even what we do know concerns their numbers alone. Whether there are differences in their constitution is a matter upon which we have no information whatever.

There is no doubt that the numbers of platelets found in a preparation of blood vary within very wide limits. Sometimes we find none at all in an entire film of blood, and at other times they are present in considerable numbers and in large clumps. Certain of these differences are, no doubt, due to differences in the method by which the blood is obtained, and it may be said generally that the more rapidly the film is prepared, the greater the number of platelets that will be found.

But methods of preparation will not account for all the differences met with. There is no doubt that in some cases the blood contains larger numbers than in others. Apart from questions of thrombosis, to which reference has already been made, the best established point is that in the afebrile anæmias (especially when there are signs of regeneration of blood), in leuchæmia, and after hæmorrhage, they are increased in number. In febrile conditions they are said to diminish in numbers, but this point does not rest upon so satisfactory a basis.

SECTION II

THE HEART AND PERICARDIUM

In this section we shall consider the changes affecting the heart and pericardium, the arteries, the veins, and the lymph channels. In most instances all of these parts of the vascular system are affected together, but for convenience of description they will be taken in the order that has been given above.

(1) THE PERICARDIUM

We may leave entirely on one side all consideration of abnormalities of the pericardial sac that result from errors in development, by reason of their extreme rarity; the morbid conditions that affect the pericardium then practically resolve themselves into the different forms under which inflammation of the serous sac shows itself. We shall, therefore, discuss in order (1) acute pericarditis, (2) chronic pericarditis and certain allied conditions, (3) tuberculous pericarditis, and (4) suppurative pericarditis.

(1) **Acute pericarditis.**—A pericardium which is acutely inflamed shows certain macroscopic changes at a very early date. The first change is probably a congestion of the blood-vessels alone, but this condition is never seen because the exudation and migration of cells, which follow immediately upon the onset of inflammatory congestion, so rapidly supervene. Hence the earliest appearance that we get is one of a congested membrane which has lost the peculiar shiny appearance characteristic of a moist but normal serous membrane. This modification is due to the presence of a small amount of fibrin which has separated from the exuded fluid and which covers the entire pericardial surface. If the case be seen sufficiently early, it will be found that the formation of this fibrinous deposit does not occur at the same time over the whole of the pericardium, but earliest at the base

of the heart and around the roots of the great vessels. In some cases, however, it appears first about the apex of the heart.

In the course of a short time, which varies according to the severity of the inflammation, the entire pericardial surface, visceral and parietal, becomes covered with a layer of fibrin. The thickness and general appearance of the deposit vary to a considerable extent. Sometimes we only meet with a thin and fairly evenly distributed layer; this is in cases of extreme severity and rapidity, further evidence of which is probably afforded by the existence of numberless petechial hæmorrhages beneath the visceral layer of the membrane and along the lines of the cardiac blood-vessels. In other cases there is a large depth of fibrin between the two layers of the pericardium which loosely binds them together by the meshwork which it produces.

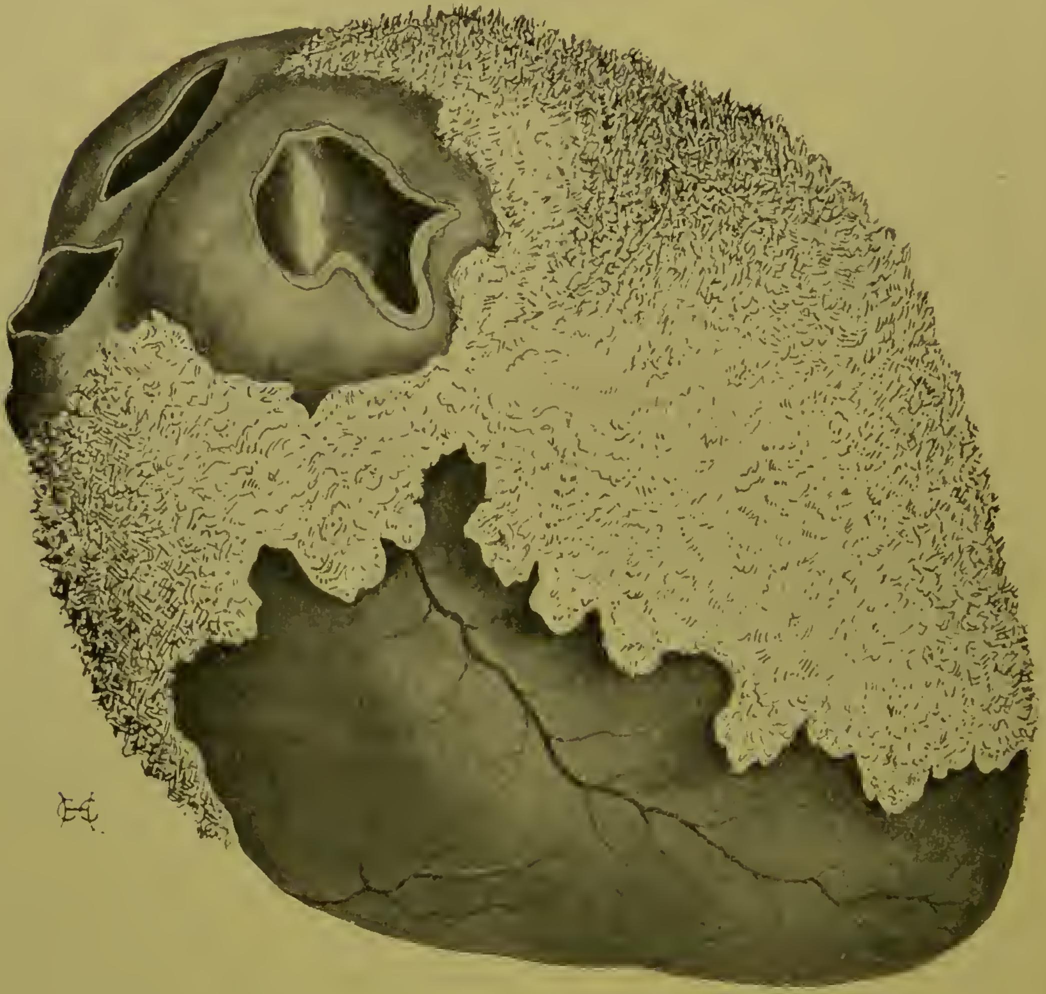


Fig. 61.—Pericarditis. Natural Size.

A heart covered with shaggy fibrin, part of which has been stripped off to show the fairly smooth visceral pericardium beneath.

Each of the two appearances mentioned in the preceding paragraph is of fairly common occurrence, but it is perhaps more usual to meet with a condition that lies somewhat between the two extremes. Thus we meet with pericardia in which both visceral and parietal layers are covered by a shaggy deposit of fibrin (unfortunately, often spoken of under the name of 'lymph'), of perhaps an eighth of an inch in thickness, and separated for the most part by a small amount of fluid. The appearance of the pericardial surfaces has then been aptly likened to that of two slices of buttered bread which have been pressed together and then drawn apart. The pericardial modification is no doubt due to the variations of the heart during systole and diastole. The two forms of inflammation are often spoken of as **fibrinous** and **hæmorrhagic** pericarditis.

In the majority of cases it is possible to strip off the layer of fibrin quite easily, and then the smooth shining surface of the serous membrane is seen beneath. It is also possible to show, if special precautions are taken, that in a large number of cases the endothelial cells which line the serous sac are still present beneath the layer of fibrin. But this is not always the case, and when the pericarditis is going to pass into a chronic condition, with the formation of definite fibrous tissue between the two layers of the sac, the endothelial cells disappear. Under any circumstances, as will be seen later, the sub-pericardial fatty tissue and the muscular tissue of the heart itself show that they share in the process by the presence in them of a great number of leucocytes.

The amount of fluid poured out by the inflamed pericardial vessels varies very greatly. In spite of the fact that it is common to speak, clinically, of a 'dry' pericarditis, such a condition never actually obtains, and the physician only signifies by the expression that so small an amount of fluid has been poured out that it is possible for the two layers of the pericardium to rub against one another and produce a 'friction rub.' In such a case, when the pericardial sac is opened, one of two conditions may present itself. Either the amount of fibrin deposited is so minute that the surfaces of the sac look dry (the inflammation being in a very early stage), or the amount of fibrin is considerable, and a felty meshwork fills up the space which normally is present between the two layers. In the latter case it is only necessary to remove some of the fibrin and squeeze it, to convince oneself that fluid is present, and present in considerable amount.

Pericardial effusion.—Sometimes, however, the amount of fluid is so considerable that its presence dominates the entire clinical picture of the condition. We then have to deal with a pericardial 'effusion.'

In pericardial effusion the fluid present distends the pericardial sac so that it takes on the shape of a pear with the base downwards. This shape is, of course, dependent upon the normal anatomical boundaries of the sac. The actual amount of fluid poured out varies somewhat, but it may generally be measured by the pint. The more slowly it is poured out the greater the accumulation is likely to be. The reason for this is that the pericardial fibrous tissue is able to undergo a gradual stretching to accommodate the fluid. In cases of pericardial effusion of this description the visceral and parietal layers of the sac are always covered by a layer of fibrin, and as a rule the layer is thick and very shaggy. Frequently, too, detached masses of fibrin are to be found floating free in the fluid.

Hydro-pericardium.—A condition exists in which there is a considerable excess of fluid in the pericardial sac, but in which the cause is not inflammatory. It is often termed 'hydro-pericardium' and arises in connection with diseases which interfere with the circulation of blood through the heart. The particular condition with which it is bound up is incompetence of the tricuspid valve and the general venous congestion to which that incompetence gives rise. It is, therefore, in essence, an œdema of passive congestion. As a rule, fibrin is not formed in the fluid which accumulates, and in particular the surfaces of the pericardium are smooth and glistening. Nevertheless it is not uncommon to find small flakes of fibrin floating free in the fluid.

Hæmo-pericardium.—Another condition which is exactly the same as far as the symptoms are concerned which it produces, is that in which a quantity of blood is poured out into the pericardium. Such a condition is always produced with great suddenness and results generally from the rupture of an aneurysm affecting the intra-pericardial portion of the aorta. But it may, of course, result from rupture of the heart, whether as the result of disease or of injury. Soon after the blood has been poured out it coagulates, but the coagulation is not the cause of the fatal event which supervenes, for death occurs almost immediately, and in any case before the effused blood has had time to clot.

Microscopic changes in pericarditis. — The microscopical appearances of a pericardium which is the seat of an early inflammation are quite typical. Starting from the external surface and considering a section of the visceral pericardium, we find that there is first of all an irregular layer of fibrin. This fibrin stains poorly with the ordinary dyes such as logwood, but if stained by gentian violet after Weigert's method, it takes on a deep violet colour. It is generally difficult to make out the existence of a definite meshwork of fibrin, owing to the fact that the strands have swollen up in the exudation fluid. As a consequence, the fibrinous deposit has a homogeneous appearance, and forms irregular prominences above the general level of the pericardium itself.

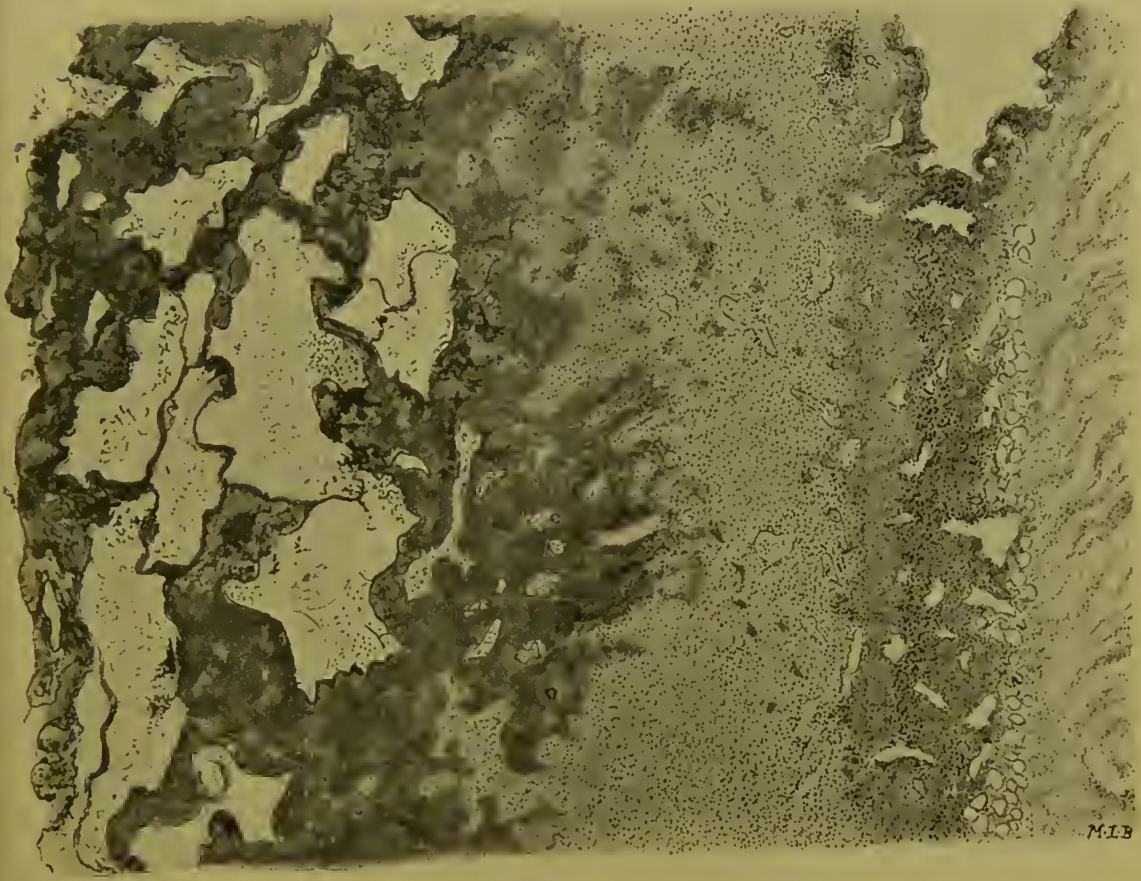


Fig. 62.—Section of Organising Pericarditis. × 12.

The figure from left to right shows the entire thickness of the altered pericardium. On the right of the figure is a layer of heart muscle, to the left of which is a thin line of sub-pericardial fat. Further to the left is a band (dark) constituting the fibrous tissue of the pericardium. This and the slightly paler band to the left (where the endothelial layer was formerly situated) show numerous newly formed blood capillaries, and some capillaries are present in the still paler and broad band containing many nuclei. The latter band consists of very young fibrous tissue with many leucocytes. The left half of the figure consists of a deeply staining and irregular meshwork of fibrin.

Beneath the layer of fibrin we generally meet with a fairly well-preserved layer of endothelial cells, but the layer is very apt to be interrupted in places. Beneath this, again, there is a small amount of fibrous tissue in which run a number of engorged capillary blood-vessels. These two layers constitute the pericardium proper, and in the normal state they are of inconsiderable thickness. But in pericarditis, owing to the congestion, the imbibition of exuded fluid, and the presence of migrated leucocytes, the thickness becomes much greater.

Beneath the pericardium proper there comes a layer of epicardial fatty tissue. This layer varies greatly in thickness, but in any case, in pericarditis, it shares in the process. For it is the seat of a marked infiltration with leucocytes, and at the same time, if petechial hæmorrhages have taken place, it is in the epicardial fatty layer that we find them most marked.

Deeper still we come upon the heart muscle itself, and it is very rare indeed to find that it has entirely escaped. In it signs of inflammation are, as a rule, conspicuously present, only the physical characters of the tissue allow of a less marked congestion and the accumulation of a much smaller amount of exudation. The number of leucocytes present in the inter-muscular fibrous septa is, however, often very considerable.

The causes of acute pericarditis are numerous. In a sense pericarditis is, most probably, always secondary. That is to say, it does not start into existence as a substantive disease, but arises during the course of another disease. Sometimes, it is true, the pericarditis appears to begin the illness, but that it does so in reality is a view that can hardly be accepted. In a less strict sense we may, however, speak of a primary pericarditis to distinguish that condition from one in which the inflammation commences, say, in the pleura and extends thence to the pericardium. This latter form of pericarditis we should then speak of as secondary.

It is probable that most forms of pericarditis are dependent upon micro-organisms. That this is so in certain cases we know. Thus we find pneumococci in the pericardium and in the exudation when the inflammation has extended to the pericardium from the pleural cavity, and it has recently been shown that in a large number of cases of rheumatic pericarditis a form of diplococcus can be isolated in pure culture from the pericardial fluid. So, too, in the rare cases in which the pericarditis is traumatic, there can be no doubt that bacteria play the chief part in instituting the inflammatory process. In other cases the matter is not so clear. Thus we meet with pericarditis in cases of renal disease, and though it is true that the subject has not been fully investigated, it is quite conceivable that the irritant is a chemical and not a bacterial one.

So far as diseases are concerned during the course of which pericarditis is likely to supervene, undoubtedly the most important is acute rhematism. Speaking roughly, nearly two-thirds of the cases of pericarditis occur during the course of this disease. The next most important cause is renal disease, and chronic renal fibrosis plays a more considerable part in the production of pericarditis than the acute varieties. Nevertheless, pericarditis, often in conjunction with pleurisy, is not infrequently met with in cases of acute nephritis. Other causes of pericarditis, but coming far behind those which have been mentioned in point of frequency, are the various acute specific fevers, and pyæmia; amongst the former scarlatina, variola, and typhoid fever are the most important.

(2) **Chronic pericarditis.**—Practically the only condition under which we meet with chronic pericarditis is that in which the two layers of the serous sac are united to a greater or less extent by adhesions. As a result, the cavity of the sac is correspondingly obliterated. This condition is known as adherent pericardium, and, as may have been gathered from what has just been said, the degrees of adherent pericardium are very various. In the majority of cases the entire cavity of the sac is obliterated. This depends upon the fact that a pericarditis almost always affects the entire sac. Rarely, however, we meet with conditions in which the two layers are joined together by a number of fibrous bands of sufficient length and flexibility to allow of the existence of a certain amount of gliding movement between the two layers.

In many cases of acute pericarditis we find the two layers of the pericardium are adherent in the sense that they are in contact with one another, except for the presence of a small amount of fibrin between them. But this is not what is meant by the term 'adherent pericardium.' By that name it is signified that the bond of union between the layers is composed of definite fibrous tissue. That this fibrous tissue is only a sequel to a condition of acute pericarditis is no doubt true, and the manner of its formation is exactly the same as what we observe in the formation of a cicatrix or a fibroid pleurisy, both of which we have already considered in some detail.

Macroscopically it is often at first unrecognised that we have to do with an adherent pericardium; it is only when the point of the scissors is found to have entered a cavity of the heart instead of the pericardial sac that the matter becomes clear. The actual thickness of the conjoined layers and the tenacity with which they adhere to one another are subject to great variation.

Microscopically, the appearances are those of a cicatricial fibrous tissue, excepting that in the majority of cases a somewhat larger number of newly formed blood-vessels is present. Foci of leucocytic accumulation are generally to be seen in various parts of the mass, and there is no evidence of the endothelial cells which formerly existed.

When the layers of the pericardium have been adherent for a very long time, and when, consequently, the fibrous tissue of which they have come to consist has become very dense, it is common to find that calcium salts have been deposited. In most cases, this calcification stops short at a point at which plaques of small size are formed in the thickened and adherent layers, but sometimes the amount of calcification is so great that the heart becomes encased in a veritable shell of lime salts. Such a shell is, of course, not entirely continuous, for under those circumstances it would be impossible for the heart to contract and dilate; but the rigidity of the heart-wall may be thereby so considerably increased that continuance of its action is wellnigh inexplicable.

In this connection mention may be made of an appearance which is very common, and which consists in the presence of localised thickening of the visceral pericardium. These localised thickenings are known as ‘ milk-spots ’ or ‘ corns.’ The chief situations in which they are found are the anterior aspect of the right ventricle and the region of the apex of the left. By some authors they are spoken of as examples of chronic pericarditis; but although it is impossible to deny that they may have been preceded by a condition of inflammation, there is no evidence that such has really been the case. For this reason it is better to class them among the chronic fibroses. Microscopically they consist of a localised mass of fairly dense and avascular fibrous tissue covered by an intact layer of endothelial cells. The situations in which they are found suggest their analogy to ordinary callosities upon the hands and feet.

(3) **Tuberculous pericarditis.**—This form of pericarditis is not met with nearly so frequently as the others which have been described. Both in its macroscopic and in its microscopic characters tuberculous pericarditis has more resemblance to the chronic than to the acute form of inflammation, for the two layers of the sac are generally found to be adherent to one another. The combined thickness of the layers is, however, much greater than is commonly the case with a simple adherent pericardium; they

may measure an inch in thickness, for example, while it is very unusual for the thickened and adherent layers of a simple adherent pericardium to measure more than half an inch.

Microscopically the distinction between the two forms is easily made, for in the tuberculous variety it is always possible to make out the presence of small tubercles, some of which are likely to be caseous in the centres. The condition, indeed, commences by the formation of minute tubercles on one or other of the pericardial layers. Most commonly it is the parietal layer that is first affected, the disease spreading from a focus of tuberculous disease in the lung or in the bronchial or infra-tracheal lymphatic glands. The condition is therefore almost always a secondary one.

Not infrequently it is found that, whereas the major portion of the pericardial sac is obliterated by the presence of the newly formed and tuberculous granulation tissue, yet loculi exist which contain a curdy or a creamy fluid. This fluid is really nothing more than broken-down caseous material.

(4) **Suppurative pericarditis.**—This condition is decidedly rare. It is of especial interest from the point of view of its causation.

Leaving on one side those cases in which a suppurative pericarditis depends upon the fact that pus formed in another organ has burst into the pericardial sac (e.g. an abscess of the liver), there is no doubt that in a certain number of cases a pericarditis arises which is associated with the formation of pus from the first. In many cases we can definitely associate the pericarditis with an antecedent suppurative pleurisy (empyema), but sometimes we find that the pericarditis arises at the same time as the pleurisy, and that it is possible to cultivate from both the same micro-organism, viz. the diplococcus of pneumonia. When dealing with the subject of peritonitis we shall have to point out that a considerable number of cases exists, particularly in children, in which no other cause can be found than the same diplococcus. Whether the pericardial affection is always to be met with along with a pleural affection, and whether the pericardial affection is ever primary while the pleural suppuration is secondary to it, are questions to which no definite answers can at present be given.

Other morbid conditions affecting the pericardial sac than those which have been mentioned are of extreme rarity. Very occasionally we meet with a pericarditis induced by the presence of nodules of new-growth, but these are always secondary. Hydatid cysts, too, have been found in this situation.

(2) THE ENDOCARDIUM

Although the endocardium lines the entire heart, it is of particular importance from a pathological point of view in those situations where it covers the cardiac valves. It will therefore be convenient to consider the valvular endocardium apart from the non-valvular. This course is the more advisable in that the changes undergone by the membrane are somewhat different in the two cases.

(A) THE VALVULAR ENDOCARDIUM

In discussing the morbid processes that affect the valvular endocardium we cannot entirely restrict our attention to the endocardium alone. For changes which occur in the cells of which it is composed always affect the small amount of fibrous tissue which lies between the layer and its reflexion. Hence consideration of the pathological anatomy of the valvular endocardium comes to signify consideration of the pathological anatomy of the cardiac valves.

Valvular changes may be acute or chronic, and although it is certain that in many instances the acute changes pass into the chronic as time goes on, there is so much difference between typical examples of the two varieties that it is necessary to consider them apart.

(1) **Acute valvular changes.**—If we leave on one side such modifications of the cardiac valves as are the result of direct injury, the acute pathological modifications of the valves resolve themselves into those which accompany inflammation. Before dealing with them it may, however, be mentioned that traumatic injuries of the valves and the chordæ tendineæ (for these structures have to be considered along with the cusps of the valves themselves) are known to exist. The injury generally consists in the wrenching of one of the cusps of the aortic valve from its arterial attachment, or in the sudden perforation of a cusp, or perhaps more commonly in the rupture of one of the chordæ tendineæ. Such an accident is likely to occur when the heart is being subjected to extreme stress. The effects of the accident upon the patient and upon the heart itself naturally vary according to circumstances, but there is nothing in the sequels different from those occurring in a similar accident produced as result of disease. They will, therefore, not delay us here.

The appearances of a valve that is the seat of acute inflammation are very variable. At a very early stage one finds the valve somewhat redder than normal, and on close examination discovers the presence of a row of minute, translucent, beadlike projections upon the surface of the valve a little distance from the free edge of the cusp. These projections are known as 'granulations,' and their actual position upon the valvular cusp is of importance from the point of view of their origin. They always are found upon that surface of the valve which lies next to the direction of the current of the blood, and are situated upon the individual cusps along the lines at which each cusp comes into contact with its fellows when the valve is closed. Hence they are found, when affecting the mitral valve, upon the auricular surfaces of the cusps, and, when affecting the aortic valve, upon the internal aspect.

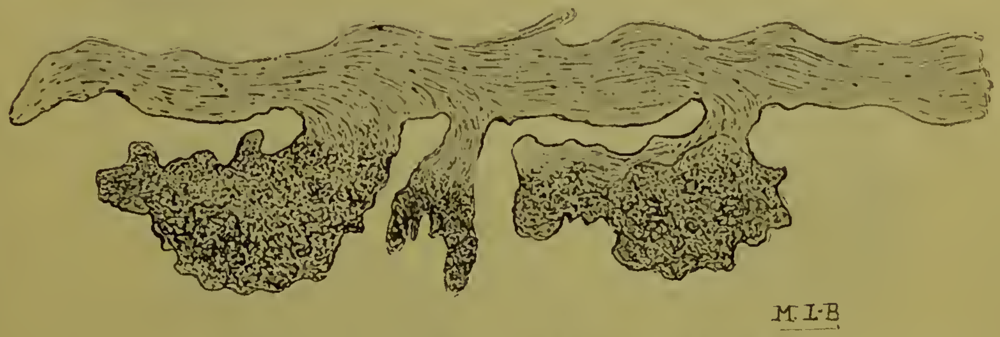


Fig. 63.—Section of Aortic Valve with Vegetations. × 6.

The valve itself and the base of the vegetations consist of dense fibrous tissue; the main portion of the vegetations consists of blood clot and fibrin.

It is not very uncommon to meet with granulations of so early a date, and when an opportunity arises for their microscopical examination they are found to consist of nothing more than an accumulation of proliferated endothelial cells, with, in some cases, a few micro-organisms. Whether micro-organisms are always concerned in the formation of granulations upon the valves of the heart is a matter upon which no certain answer can as yet be given. It is certain that their presence cannot always be demonstrated, but it is well in accordance with modern views of pathology that the existence of a bacterial irritant should be an excessively common, if not an absolutely necessary, feature in their formation.

The proliferated cells of which the granulations consist are at a disadvantage in regard to nutrition, and soon undergo degenerative changes which are probably fatty in their essence. As a result the most superficial cells break down and an irregular surface is exposed to the blood. Fibrin is therefore deposited upon the roughened surface, and we find masses attached to the valve which consist of a few endothelial cells capped with fibrin. Such formations are termed 'vegetations,' and even when no larger than a pin's head their constitution is that just given. On the other hand, it is very common to find vegetations of a much larger size, sufficiently large and numerous, indeed, to obstruct the orifice at which the valve is situated to a remarkable extent, and to earn for the particular form the name of 'vegetative endocarditis.'

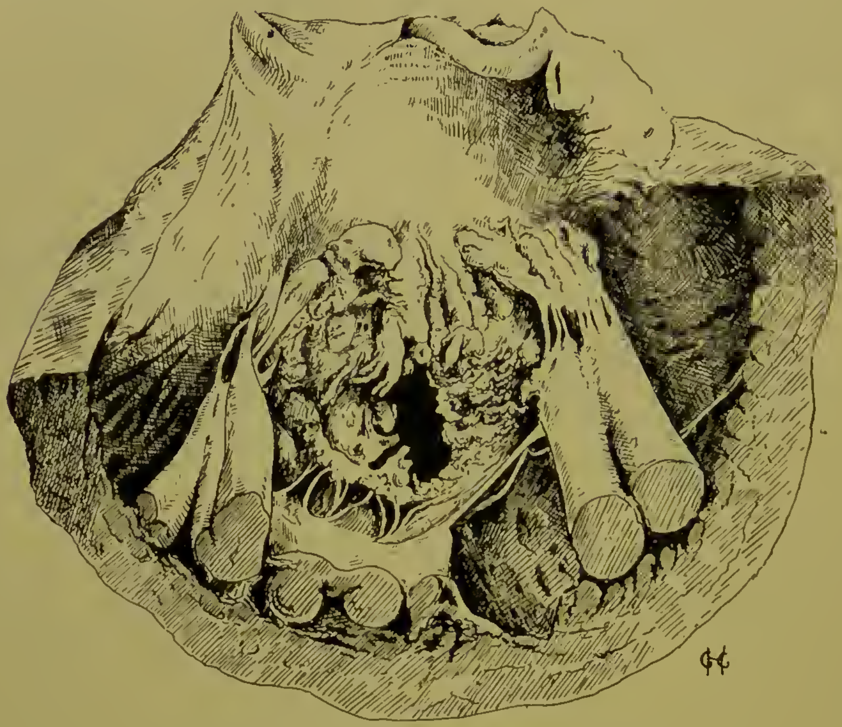


Fig. 64.—Vegetative Endocarditis. × $\frac{3}{4}$.

The mitral orifice viewed from below. Vegetations are present on the edges of the flaps and on certain of the chordæ tendineæ. The vegetative condition is acute. The chordæ tendineæ, though somewhat shortened, are not thickened.

Microscopic examination of a valve upon which a small vegetation is situated, however, shows that the condition is not quite so simple as might appear from the considerations just given. For it is then seen that the fibrin itself is of different constitution in different places. At one it is fibrillar and forms a dense meshwork, similar to that which we are accustomed to recognise as signifying the formation of fibrin. At another place the fibrils have swelled up, presumably by imbibition of fluid from the blood by which they are bathed, until they form definite fibres of some thickness which have a finely granular appearance.

And yet again in other places they have become transformed into a homogeneous material of hyaline structure, which has little or no resemblance to the fibrin from which it was formed.

At the same time the substance of the valve itself has undergone alteration. Normally it consists of a dense fibrous tissue in which connective-tissue corpuscles are few and small, but now the fibrous tissue has undergone a hyaline modification, the presence of fibroblasts is to be noted, and in places small numbers of leucocytes are to be seen. In addition, it is probable that at various points accumulations of red blood corpuscles recalling hæmorrhages will be present. These collections of red cells are small masses of clot which have been entangled among the meshes of the fibrin during its deposition. With regard to the presence of micro-organisms, nothing further can be said than was said in reference to their presence in the granulations; they may or may not be found. It must be noted, however, that they may be present in masses so dense that their presence is overlooked, and also that micro-organisms may be found upon the surface of the vegetations which have been deposited or have multiplied there during the last hours of life or after death, and which have had no causal relationship with the formation of the vegetations at all.

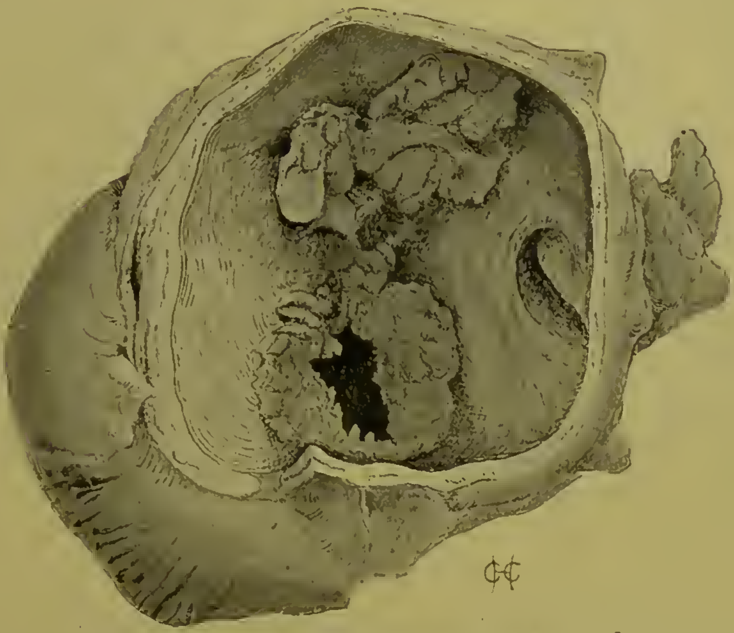


Fig. 65.—Vegetative Endocarditis. × $\frac{3}{4}$.

The same specimen as fig. 64 viewed from above. The degree of stenosis of the mitral orifice, the fibrin deposited on the auricular surface at a distance from the mitral orifice where the regurgitant column of blood from the ventricle impinged, and the hypertrophy of the auricular wall dependent upon the stenosis are well shown.

To both of the conditions which have been described above the name 'acute endocarditis' is given. Formerly they used to be termed *simple* to distinguish them from another form of endocarditis to which the name *ulcerative* was applied. At the present time, although we still speak of ulcerative endocarditis, the term *simple* has largely been given up.

Ulcerative endocarditis.—Ulcerative endocarditis forms so important a variety of the entire group of valvular affections, that it is necessary to give to it a special description.

If we bear in mind the definition of ulceration that was given earlier and remember that it was said to be a form of molecular degeneration or necrosis, it will be clear that no *essential* difference obtains between the form of endocarditis described above and that with which we are now concerned. The difference is one of degree only. For whereas in simple acute endocarditis the ulceration is confined to the surface of the granulations only, in ulcerative endocarditis it extends deeper, and indeed often leads to a considerable loss of substance of the valve. As a result it is not uncommon for individual cusps to lose entirely their normal appearance, and to become converted into a more or less shapeless mass, which may be adherent at its base by the normal amount of tissue, or may have ulcerated therefrom to a considerable extent and swing loosely in the blood current.

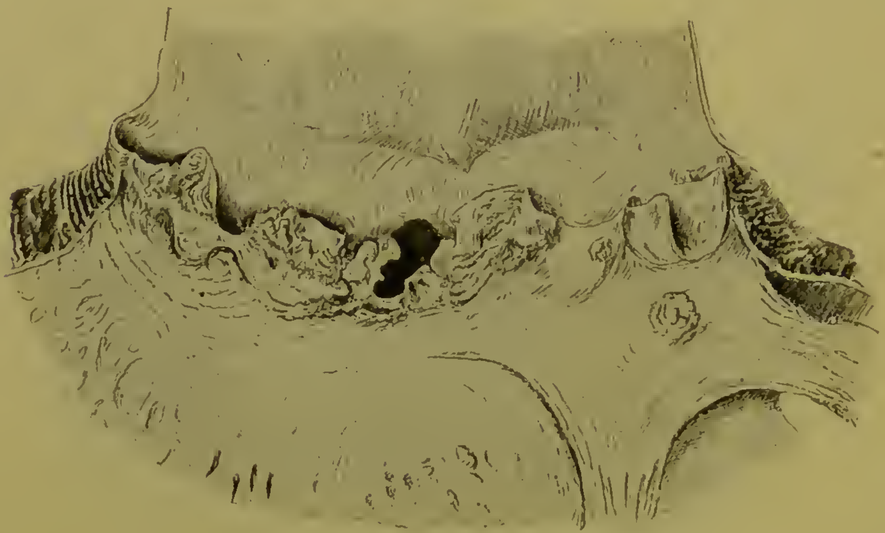


Fig. 66.—Ulcerative Endocarditis. Natural Size.

The aortic valves are shown ragged and eroded. The dark spot in the centre shows where ulceration has taken place, both of the valve itself and of the tissue of the aorta in the sinus of Valsalva behind the valve.

Owing to the large amount of valve tissue which has been damaged, the liability to the deposition of fibrin from the circulating blood is proportionately increased. As a result it is common for the ulcerative form of endocarditis to be largely associated with the vegetative. This is merely another indication of the fact that there is no intrinsic difference between them.

One point with regard to ulcerative endocarditis must be noted. It is that micro-organisms are always to be found in, and in many instances can be cultivated from the vegetations on the damaged valves. These micro-organisms are of different kinds, but speaking generally it may be said that they usually belong to the class of pyogenetic cocci, and amongst these streptococci or diplococci (growing in cultivation either as streptococci or as diplococci) are the most common. Thus it has been proved that *Streptococcus pyogenes*, *Micrococcus gonorrhœæ*, and *Micrococcus pneumoniæ* are associated with the condition. *Staphylococcus pyogenes aureus* has also been found in the ulcerated valves, but much less commonly than *Streptococcus pyogenes*.

An important point in reference to ulcerative endocarditis is the fact that portions of the injured valve or of the fibrin which is deposited upon it, or of the bacteria which are multiplying there, are liable to be detached and carried into distant parts by the blood stream. As has already been said when considering the questions of embolism and infarction, the same may occur in a simple case of endocarditis. But the difference is that the virulence of the bacteria which are thus carried to distant parts shows itself at the points at which the emboli become lodged no less than at the seat of their formation on the valve. That is to say, embolism is a particularly common occurrence in cases of ulcerative endocarditis, and the results of the embolism are especially severe. For the micro-organisms being so commonly pyogenetic, the result of the embolism is the formation of an abscess instead of a mere aseptic infarct; a close relationship between ulcerative endocarditis and pyæmia becomes manifest.

Into the microscopical appearances of a valve affected by ulcerative endocarditis there is no need to enter. For they are those found in any case of simple endocarditis, with the additional fact that the destruction of tissue and the number of leucocytes present are greater. Nor need we delay over the histological features of the pyæmic abscesses produced as the result of embolism. It need only be said that there is a tendency for the abscesses to be more irregular and to have more ragged walls than is the case with an abscess formed apart from the cardiac condition. It must, however, be mentioned that the myocardium itself manifests evidences of participation in the process. Although this is not the place to refer to the point, it is convenient to state that the cardiac muscle fibres generally are the seat of a cloudy swelling with a loss of their striation and translucent appearance, and may be the seat of fatty change.

One other point also calls for remark. There is no doubt that it is more common to find the ulcerative process in a heart the valves of which were previously diseased. Hence, in addition to the acute and ulcerative changes which we find in the valve, there are also present more or less marked signs of antecedent, and chronic, endocarditis. But, although this statement is undoubtedly true in a large majority of cases, examples are met with in which the endocarditis is ulcerative from the first. Amongst these cases we have to differentiate (1) those in which the disease which was first, apparently, a simple condition, gradually merges, in the course of weeks, into the ulcerative, without there being any possibility of indicating when the change from simple into ulcerative took place, and (2) those cases in which the disease is ulcerative from the first. That such cases obtain we have full reason for believing, but they are extremely rare.

Aneurysm of valves.—A condition of the cardiac valves which may fitly be considered here is that of aneurysm. Upon the general subject of aneurysm we shall have to say more later, but it may be said that an aneurysm is a localised dilatation of the wall of a blood-containing cavity as the result of the blood pressure on a weakened spot. In the case of the heart we have to recognise two kinds of aneurysm, those of the muscular walls and those of the valves. Concerning the former nothing will be said here, but aneurysms of the valves find here their proper place. For they are almost always the result of ulcerative endocarditis. The method of their formation is as follows. Owing to the local ulceration which commences upon one side of the cusp, there is produced a local weakening which under ordinary circumstances would rapidly go on to definite perforation. When an aneurysm is about to be formed, however, the ulcerative process stops short of perforation, and the cusp is therefore left with a larger or smaller portion of its surface greatly diminished in thickness and proportionately less capable of withstanding the pressure of the blood column which it is normally called upon to resist. Being composed of fibrous tissue, it therefore yields to the pressure, and its elasticity being small normally, and being under the circumstances still further diminished by the inflammatory processes to which it has been exposed, there is little or no tendency for the valve to resume its former shape when the pressure of the blood column is taken off. Little by little, therefore, a sac is formed over the weakened portion of the cusp.

Aneurysmal dilatations of the cardiac valves are not of common occurrence, nor are they large when present. They are most commonly found to affect the mitral and aortic valves, and of these the mitral cusps are the more commonly affected owing to the fact that they are thicker in their texture and are consequently less liable to perforation. When an aneurysm affects the aortic cusps, the actual thickness of the affected cusp has almost always been largely increased by the deposition of a considerable amount of fibrin, or by the formation of inflammatory fibrous tissue.

(2) **Chronic valvular changes.**—Chronic changes affecting the valvular endocardium are of two distinct kinds so far as their ætiology is concerned. They may either be sequels of an antecedent acute change or they may not have been preceded by any acute valvulitis so far as we are able to determine. The appearances presented by the altered valves under the two sets of circumstances are also different.

In cases in which the chronic valvular affection is the sequel of an antecedent acute change, the injured valve is repaired by the formation of cicatricial tissue. This cicatricial tissue, following its natural course, contracts as time goes on, and the result is that the orifice of the valve becomes stenosed, the cusps of the valve, instead of consisting of a thin and delicate layer of connective tissue, become converted into a more or less irregular mass of dense scar tissue, and the free margins of the cusps, instead of being able to appose themselves perfectly to the margins of their fellows, become thick, hard, and rigid. To what extent these changes manifest themselves depends upon circumstances, and especially upon the degree of the injury which the valve has undergone when it was subject to the acute inflammation. In the majority of cases the contraction of the valvular opening is considerable, and in some cases (e.g. extreme mitral stenosis) the orifice of the valve is converted into a mere chink, the edges of which are guarded by a ring of dense fibrous tissue which bears little or no resemblance to the cusps which it represents.

Nor is this all. For just as scar tissue in other situations is liable to become the seat of the deposition of calcium salts, so the altered and formerly inflamed valve may become converted into a ring of tissue which varies in hardness between cartilage and bone. As a rule, when calcification of a valve has taken place, the immediate process ends therewith, but sometimes a deposit of fibrin takes place upon portions of the altered valve and further complicates the condition. It is probable that such deposition of fibrin only takes place during the last hours of life.

There is little to say concerning the microscopical characters of a valve that is the seat of chronic inflammatory change. The main portion of the altered valve consists of a fibrous tissue of extreme density. It contains very few fibroblasts, very few blood-vessels, and very few leucocytes. Indeed, it is mainly composed of a tissue which has a hyaline appearance under the microscope, and which, were it not for its intense hardness, might be mistaken for fibrin which had undergone a hyaline change as the result of imbibition of exudation fluid.

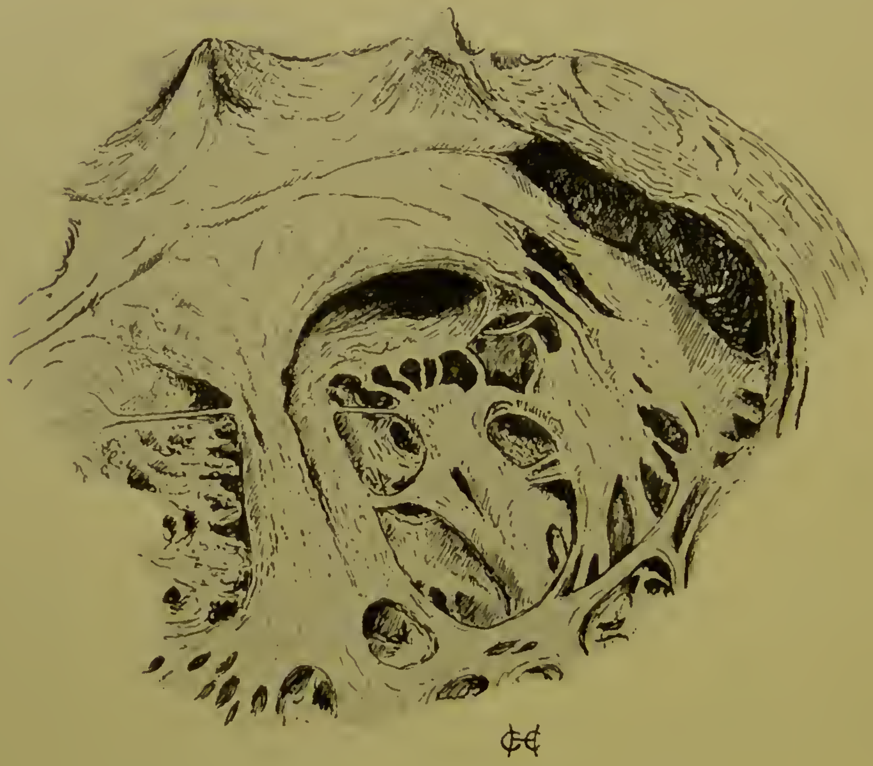


FIG. 67.—CHRONIC ENDOCARDITIS. NATURAL SIZE.

A 'button-hole' mitral orifice viewed from below. The flaps of the valve are of cartilaginous hardness, and cannot be brought into contact. The chordæ tendineæ are shortened, thickened, and, in places, coherent.

The causes of this variety of chronic valvular change are naturally those which are causes of acute changes It must be noted, however, that ulcerative endocarditis is not an antecedent, so far as we know, because it is a condition of so great severity that it is incompatible with a continuance of the patient's life for a sufficient length of time to allow of the supervention of chronic changes.

The variety of chronic valvular change which is not, to the best of our knowledge, preceded by any acute changes produces modifications of the valves which are not usually so severe as they are in a marked case of chronic inflammatory disease. As a rule, there is a thickening of the valves, and especially of their margins, but the normal outline of the individual cusps is preserved. The cusps are harder and stiffer than normal, and that is all.

One point must be noticed in which both varieties of valvular change agree. It is very common to find that the chordæ tendineæ are shorter, thicker and tougher than normal, and, moreover, that, instead of springing one by one from the summit of the musculi papillares, they are gathered together at their attachment into a dense mass of fibrous tissue. This change naturally only takes place when the auriculo-ventricular valves are affected, and it is uncertain whether it is to be looked upon as concomitant with the actual valvular change, and as being brought about by the same agency, or whether it results from the fact that the chordæ are less brought into play when chronic valvular changes have occurred, owing to the excessive rigidity of the segments of the valve.

In another chronic valvular condition which it is believed is independent of antecedent inflammation, calcification is the prominent feature. It is probable that in most instances the calcification has been preceded by the occurrence of atheroma. That this view is correct is rendered the more probable in that the valve which is most commonly affected by the calcareous change now under consideration is the aortic, and it is well known that, of all the regions which are affected by atheroma, the orifice of the aorta is the most common.

The chronic valvular changes which supervene upon acute inflammation are naturally to be met with at all times of life at which acute valvulitis is common, and since it is especially the young who are subject to acute changes, it is especially the young and those who have reached to middle life that are subjects of chronic inflammatory valve changes. But the case is different with the chronic changes we are unable to connect with antecedent acute inflammation. For these are particularly liable to affect persons of advanced years, especially that form in which calcification is a prominent feature. Antecedent syphilis, too, is an important factor, by way of the degenerative changes which it very commonly induces in the lining of blood-vessels and in the causation of atheroma generally.

Amongst chronic changes which affect the valves we must also make mention of the occurrence of localised foci of fatty change. Such foci are not at all infrequently met with, and in a large number of cases they are regarded as being due to atheroma. That in certain cases they are really manifestations of this degenerative change there is no doubt, but frequently there is considerable difficulty in thus considering them. Thus they are to be found upon the valves of infants, and not only so but also under conditions in which no other evidence of atheroma obtains. The commonest situation for them is the aortic flap of the mitral valve. Under the microscope the valve at the point of their situation is found to be a little thicker than the rest of the valve, and to contain a considerable number of fat globules. Whether the condition has any pathological significance is unknown.

Before passing entirely from consideration of the valvular pathological conditions, it is necessary to consider for a moment the ætiological factors inducing them and the relative frequency with which the different valves are affected.

So far as ætiology is concerned, a few points have already been touched upon, but it may be said shortly that, of all the causes of valvular affections, the most important by far is acute rheumatism. Perhaps the liability of valvular lesions to be due to this disease is not quite so great as in the case of pericarditis, but it does not fall far short. On the other hand, renal disease, which is a fairly common cause of pericarditis, is practically without effect upon the valves of the heart. Next to acute rheumatism as a cause of endocarditis come the various septic conditions which lead to an acute endocarditis of the ulcerative type, but, as has already been said, this condition is most frequently superposed on an antecedent valvulitis, whether acute or, as is more frequently the case, chronic. Of about the same frequency as a cause is chorea, a disease which, although very uncommonly associated with pericarditis, is nevertheless frequently associated with endocarditis. Chorea and acute rheumatism have numerous affinities of which the tendency for the occurrence of acute valvular changes is only one, and recent work has rendered it possible that they are closely allied, so far as ætiology is concerned, if, indeed, they do not both depend upon the same bacterial agent, of which they are only slightly different manifestations.

To the importance of syphilis in the ætiology of some of the chronic forms of valve disease reference has already been made.

The valves of the heart are not affected with the same frequency. Thus it is far more common for disease to be present in the valves of the left side of the heart than in those of the right. In fact, the right-side valves are so rarely affected that we may say with practical certainty when an example of the condition is found, that it is either due to a general pyæmic infection such as occasions the ulcerative type of endocarditis, or that it was due to infection of the heart while the fœtus was yet *in utero*. Nor are the valves on the left side of the heart affected with equal frequency, for the segments of the mitral valve are far more commonly found to be diseased than those of the aortic valve. The same relative frequency obtains in the case of the valves of the right side of the heart, for, putting the conditions which are included under the general name of 'congenital heart disease' out of the question for the present, the tricuspid valve is more frequently affected than the pulmonary.

In a large number of cases the endocarditis is not confined to one valve. Thus aortic disease and mitral disease are met in conjunction with one another with frequency, and in ulcerative endocarditis it is not very uncommon to find that, in addition, the tricuspid valve is affected also. So far as the association of pericarditis with endocarditis is concerned, though one frequently meets with cases in which there is marked endocarditis in the complete absence of pericarditis, the two conditions are often present together.

(B) THE NON-VALVULAR ENDOCARDIUM

In some respects the affections of the non-valvular endocardium are similar to those of the membrane when covering the valves, but in others they are quite different. Thus, although we can have no doubt that when a condition such as acute rheumatism is in existence and is producing valvular changes, the non-valvular endocardium must be similarly affected in some degree, there is never produced so marked a modification. The utmost that we find is an extension of the acute process from the valves to that portion of the endocardium covering the muscular wall of the cavity in question. Here we may undoubtedly find a deposition of fibrin which is in every point comparable with that which occurs upon the valves themselves, and at times the area affected is considerable. But with this condition the acute modifications of the non-valvular endocardium are practically exhausted. We only have to add that, when the myocardium itself is the seat of suppuration which extends towards the cavities of the heart, the endocardium immediately superincumbent is, naturally, the seat of acute change.

On the other hand, the non-valvular endocardium agrees with the valvular in its liability to the occurrence of chronic changes. Even these are not very common, but there is no doubt that a condition obtains in which the entire membrane becomes thick and semi-opaque. This change is exactly the same as that which leads to the stiffness and rigidity of the valves to which reference has already been made, and the histological appearances in the two cases are also the same. That is to say, the thickened endocardium consists of an increased number of layers of fibrous tissue, with a smaller proportion of connective-tissue cells. A condition of this kind is sometimes localised, though more commonly it is general. When localised it bears a manifest resemblance to the 'corns' or 'milk-spots' of the pericardium.

With regard to their clinical importance, however, these changes are far less significant than one which is to be recognised rather by its results than by its actual presence. Indeed, it is by the occurrence of the results that we are obliged, in the majority of cases, to conclude that the morbid condition of the endocardium has been in existence. The change in question is an interference with the nutrition of the endocardium at a certain point, and the result is the occurrence of thrombosis at that point.

To the subject of thrombosis generally reference has already been made, but the matter is one of so considerable importance in connection with the heart, that it must again be mentioned here.

It is very uncommon for the heart cavities to be found completely free of blood-clot at an autopsy, and even if such a condition obtains, as regards the ventricles, a certain amount of clot is almost always found in the auricles. The clot itself differs in its appearance in different cases. Without considering such conditions of the blood as that which is characteristic of leuchæmia, and in which the blood clot formed is naturally of an abnormal colour, it may be said that the varieties of coagulum met with in the heart are the red and the white. It is clear that the white coagula owe their absence of colour to an absence of red blood corpuscles in their composition.

White clots are met with under two conditions. They may be found when death has taken place with slowness, or rather when coagulation has long been delayed, and yet the circulation has been so sluggish that the red corpuscles have had time to become deposited in the vessels, and they may be formed when the blood stream is travelling at an approximately normal rate. Under the former circumstances the clot may not be actually colourless throughout (though such is commonly the case when death has been more than ordinarily lingering); it may be colourless in its superficial aspect, and deep red or purple in the dependent parts. In any case it is non-adherent, and can be drawn out from the cavities of the heart and the great vessels. Very occasionally such colourless clot may be found extending to quite small branches of the pulmonary artery.

When formation of fibrin takes place from the still circulating blood the resulting clot is always colourless, and almost always adherent to the wall of the heart itself. In a large number of cases the layer of the endothelial cells beneath the clot is completely wanting, and even in those cases in which portions of it remain it is certain that it has lost its vitality. Formation of this kind of coagulum is chiefly met with in the auricular appendices, but it also occurs over lesions in valves and damaged endocardium in their neighbourhood.

It has been said above that fibrin deposited from the still circulating blood is *almost* always adherent to the wall of the heart. The reason of this reservation is, that a condition is known in which a mass of colourless fibrin lies free in one of the cavities of the heart. Such masses are globular in shape, and for this reason they have received the name of 'ball-clots.' They occur in the auricles, and in many instances so nearly fill their cavity, and seem so well adapted for completely closing the auriculo-ventricular orifice, that it is difficult to understand how the circulation was carried on. There is little doubt that they were formerly attached to the auricular wall at some point, and were formed in the same way as other colourless clots. The explanation of their freedom is probably to be found in the fact that they were attached by a narrow pedicle, which in the course of time became broken through. That they were formerly attached is rendered certain by the fact that the existence of polypose clots is definitely known.

Occasionally coagula are met with which are completely softened in the centre. This is not infrequently the case with ball-clots, but it is also met with in cases in which the coagula are still adherent to the cardiac wall. The condition is not a very common one, and when it occurs it is always evidence that the last illness has been long and accompanied by great prostration. The material present in the centre of the mass under these conditions has all the macroscopic appearances of pus. It is a creamy fluid which separates on standing into a deposit and a supernatant fluid. Practically it has much the same indefinite histological composition as the pus from a cold abscess. That is to say, the deposit consists of granular *débris* and fat globules; it is quite sterile.

(3) THE MYOCARDIUM

The changes undergone by the musculature of the heart under pathological conditions are necessarily of great importance from the position which the organ holds in the entire economy, and the fact that its function is wholly dependent upon the nutritive condition of its muscle fibres. In many instances the myocardial changes are bound up with either pericardial or endocardial changes or with both. In other cases they are bound up with morbid conditions of the blood-vessels, while in yet a third set of cases the pathological condition of the heart is peculiar to itself, so far as our present knowledge goes. We shall consider the pathological anatomy of the myocardium under the headings of (1) Inflammation, (2) Degenerations and other retrogressive changes, (3) Changes occurring in the heart as a composite muscular organ, and (4) New-formations.

(1) **Inflammation—Myocarditis.**—Several varieties of myocarditis are known, and of these (*a*) the rheumatic (simple), (*b*) the pyæmic, (*c*) the syphilitic, and (*d*) the tuberculous are the most important.

(*a*) **Simple myocarditis.**—In all forms of myocarditis we meet with the usual evidences of inflammation as they are seen in solid tissues. Thus there are more or less well-marked infiltration of the muscular tissue with small round cells, and signs of degeneration in the muscle fibres themselves. The small round cells are of the lymphocytic type, and are evidently cells which have migrated through the walls of inflamed myocardial blood-vessels. They are found in particularly large numbers in the connective tissue that lies between the individual muscular bundles, but in cases in which they are present in extremely large numbers, and in which, consequently, the inflammation is particularly acute, they may encroach upon the muscle bundles and lie between the individual muscular fibres of a bundle.

The signs of degenerative change in the essential elements of the myocardium are commonly well marked. There is a general loss of the semi-translucency of the muscle fibres and a disappearance of their striation. As a consequence they become granular in appearance, and since they also absorb some portion of the fluid that is exuded by the blood-vessels, they are somewhat swollen. Degenerative changes of a somewhat similar kind, although they need special precautions to demonstrate them, occur in the nerve cells of the cardiac ganglia, particularly in the myocardial affections that are associated with diphtheria.

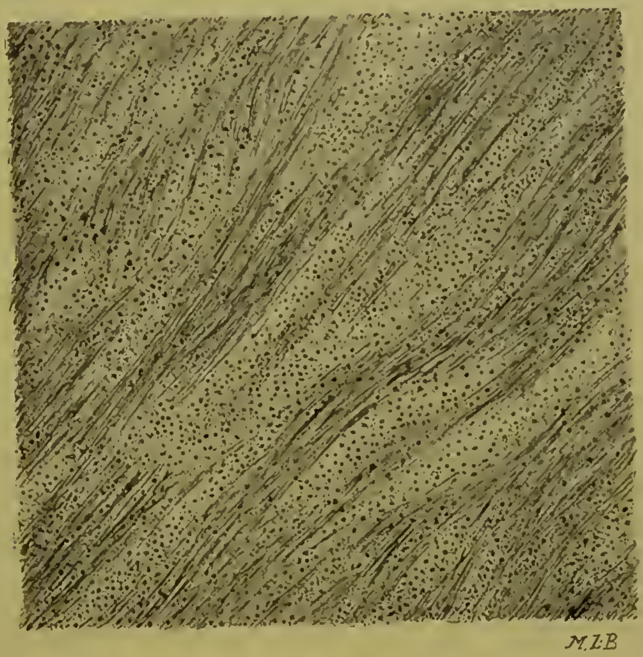


FIG. 68.—SECTION OF MYOCARDITIS. × 80.

The muscle fibres are separated by a material, intensely infiltrated with leucocytes, which apparently more or less replaces the pre-existing fibrous tissue. A general cloudy or granular appearance characterises the muscle fibres themselves.

Congestion is not a very obvious feature of myocarditis owing to the firmness of the tissue in which the inflammation is taking place. Hæmorrhagic foci, on the contrary, are fairly common, but they are rarely of large size.

The characters that have been described above are seen to the greatest extent in cases in which the inflammation is of a very acute type. Such, for example, is the case when the heart is affected during the course of an attack of acute rheumatism, or when the inflammatory condition invades the heart substance after commencing in the pericardium. To a certain extent the myocardium participates in every inflammation of the pericardium and endocardium, but the extent differs greatly. Sometimes the changes of the myocardium concern only a thin layer of tissue next to the serous surface, but sometimes the entire thickness of the wall is involved.

(*b*) **Pyæmic myocarditis.**—Pyæmic myocarditis is characterised by the fact that the inflammation is not equally diffused throughout the entire myocardium, but is localised at various points where it is so intense that it ends in the formation of a small abscess. The condition is in reality embolic, and this accounts for the fact that the process is not equally advanced at all points of the myocardium. The abscesses have the ordinary characters of pyæmic abscesses, including the presence in the pus of a relatively large number of micrococci. They rarely reach to a very considerable size owing to the severe constitutional symptoms which they induce. Nor are they commonly present in large numbers.

Myocardial abscesses are accountable for one form of the condition known as aneurysm of the heart, viz. acute aneurysm. The method of their formation is quite simple. For when the myocardial abscess increases in size, it must point towards either the pericardium or the endocardium. If it points in the former direction a suppurative, or perhaps an adhesive, pericarditis is set up ; but if it points towards, and ultimately bursts into the cavity of the heart, a localised weakening of the cardiac wall is produced, and this, yielding before the force exerted by the blood pressure, leads to the formation of a thin-walled aneurysmal sac. Such aneurysms may be formed in an outer wall of a ventricle or in the septum.

(*c*) **Syphilitic myocarditis.**—Syphilis manifests itself in the case of the myocardium in one of two forms. Either we find that there are localised foci of a chronic inflammation, or else there is a definite formation of gummata. When gummata are present they consist, as elsewhere, of an irregular mass of caseous material around the margin of which is a certain amount of newly formed fibrous tissue. The arterioles in the circumference of the mass are likely to show that morbid change in their internal coats which constitutes endarteritis obliterans. When the syphilitic manifestation does not take the form of a gumma, the appearances are merely those of a chronic inflammation with no distinctive characters. Thus we find that there is little or no caseation, that small round cells are numerous, that a large number of fibroblasts are present with a relatively small amount of fully formed fibrous tissue, and that a certain number of well-formed giant cells are present also. At the same time there is a general absence of endarteritis obliterans. There is nothing, therefore, that could serve to distinguish the syphilitic from the tuberculous or any other chronic form of inflammation. This point is well seen by comparing figs. 20 and 25. As a rule this variety of syphilitic myocarditis is tolerably evenly diffused throughout the heart muscle, whereas the gummatous is more strictly localised, although a considerable amount of the septum or of one ventricular wall may be replaced by the caseous material of a gumma. Most frequently, either the gummatous or the chronic inflammatory form of syphilis is found to affect the heart; it is rare for both forms to be met with in conjunction.

(*d*) **Tuberculous myocarditis.**—Tuberculous myocarditis calls for no special remark. It is of rare occurrence, and even when found almost always results from the extension of a tuberculous pericarditis which has itself extended from a tuberculous lung or bronchial gland. It then presents no special characters. It is a curious point with regard to tuberculosis of the heart that, although miliary tuberculosis, generalised throughout the body, is an extremely common condition, it is nevertheless one of the rarest occurrences for miliary tubercles to be found in the heart or pericardium. And this, although there is no doubt that the generalisation of the morbid process takes place by the blood stream.

(2) **Myocardial degenerations and other retrogressive changes.**—One of the most striking retrogressive changes that are met with in the case of the heart is that which has been termed **serous atrophy.** The condition is not very frequently met with in a pronounced form, but in a less degree it is common enough. It consists in the complete disappearance of the epicardial fat and the œdematous transformation of the loose connective tissue which in the normal state of the organ holds the fat globules. At the same time the heart itself is diminished in weight, so that the appearance is given of a small heart more or less enveloped in a mass of gelatinous material. The change is always met with in cases in which the patient has become exhausted and wasted by a prolonged illness, and in the majority of cases the serous atrophy is conjoined with some other retrogressive change in the myocardium, of which the commonest is brown atrophy.

The condition of **fatty infiltration** is practically the exact converse of that which has just been described. For in it there is an increase in the amount of fatty tissue in those situations in which it is normal to find some fat. The amount of excess varies within very wide limits. Sometimes it is only just possible to say that the epicardial fat is increased in quantity, at other times the overgrowth of fat is so enormous that the muscular tissue of the heart is entirely hidden. Such a condition as the last mentioned is often spoken of as **adipose heart.**

Although it is commonest to find in cases of fatty infiltration of the heart that the fatty tissue is chiefly present upon the surface of the organ, this is not its sole situation. For it will be in found, larger or smaller quantity, to have become deposited in the trabeculæ of fibrous tissue which enter the heart itself and constitute the inter-muscular septa. When fatty infiltration of the heart is extensive, it is almost always associated with some other retrogressive change. Simple atrophy from pressure and fatty degeneration of the muscular fibres are the most common. Fatty infiltration is generally associated with great deposit of fat in the tissues elsewhere.

Fatty degeneration of the myocardium is one of the commonest and one of the most serious morbid changes to which the organ is liable. It, too, varies considerably in extent, and it is only when it is present in a considerable degree that it can be recognised macroscopically. It then shows itself by the existence of a mottled appearance of the myocardium in various situations, which gives to the heart-wall an aspect somewhat similar to that presented by the breast of a thrush; for this reason this name is sometimes applied to the condition. The appearance has also been compared to that of the fur of a tabby cat, and the term 'tabby-cat striation' is frequently used to describe it.

Fatty degeneration affects any part of the myocardium, but the situation in which it is met with most frequently is the papillary muscle. Here, it may be recognised by the naked eye on the surface, but usually, if a section of the mass of muscle is made, the appearance is more distinctive. When the fatty degeneration is at all extensive, it is probable that some portions of the entire wall of the right ventricle will be found to be converted into fat.

Microscopically, fatty degeneration (fig. 6) is seen to affect individual muscle fibres, although a number of fibres in close contact will be affected by the change. Localised patches are found, if the section has been stained with osmic acid, which consist of a number of fibres in which are present so many fat globules the envelopes of which have been blackened by the acid that the particular foci of tissue affected are a dense black. In the immediate neighbourhood are muscle fibres which have not undergone the degenerative change, which therefore do not become blackened, but show up in marked contrast to the fatty portions. These portions of tissue, which are not the seat of the fatty change, are not, however, perfectly normal. There is a granular appearance and a loss of striation even in them.

The globules of fat in the degenerated muscle fibres are always small, and although it cannot be said that they are absolutely of one uniform size, they vary very little in this respect. It is quite impossible to say why there is so conspicuous a difference between neighbouring foci of muscle in the amount of fat which they contain. That the musculi papillares are the commonest seat of fatty degeneration we may, however, probably ascribe to the fact that they are the parts of the myocardium which are taxed to the greatest extent whenever any particular stress is thrown upon the organ.

The occurrence of fatty degeneration is closely bound up with circumstances which force the heart to act more frequently or more forcibly under conditions in which the supply of nutriment is diminished. . Bearing this in mind, it is easy to indicate the kind of case in which it will be found. Thus it occurs in almost all cases of pernicious anæmia, owing to the fact that the tissues at large require a more frequent renewal of blood (and therefore an increase in the rate of the heart's beat), because of the insufficiency in amount of hæmoglobin present in each unit of blood which they actually receive. But the myocardium itself is labouring under the same disadvantage as the tissues at large and cannot recoup itself by drawing on any other source. For a similar reason fatty degeneration is also found, in cases of pernicious anæmia, in the muscle fibres of the diaphragm. It is unnecessary to point out how great an effect upon the functional power of the heart, as the central pump of the vascular apparatus, fatty degeneration of the myocardium must have.

Another condition which is often found with, and is the cause of, fatty degeneration of the heart, is extensive atheroma of the coronary arteries. Such atheroma is almost always associated with calcification of the walls of the vessels in cases in which the fatty change is advanced, but that it is not a necessary accompaniment is shown by the fact that when the vessels themselves or their orifices are obstructed by soft atheroma, fatty degeneration also occurs, though it is not generally so advanced as when the vessels are calcareous. Many other conditions are known under which fatty degeneration of the heart muscle occurs, but they do not call for special notice, inasmuch as they all act after the fashion described above.

Before passing from consideration of the fatty changes of the myocardium, reference may be made to two conditions which are sometimes met with in their connection. These are **rupture** of the heart and **angina pectoris.**

Rupture of the heart is a rare accident, and, apart from actual violence, is always due to the existence of a marked degree of fatty degeneration of the myocardium. In a very considerable majority of the cases that have been recorded, the accident has affected the left ventricle, and it is at the point at which this cavity has the thinnest wall—viz. at the apex—that the rupture usually occurs. Nevertheless, rupture of the wall of the right ventricle, and rupture at other situations than the apex, have been met with.

Angina pectoris is a condition in which the principal symptoms are an agonising pain that is first felt in the præcordial region, and thence passes in other directions, most commonly down the left arm, and a sense of impending death. The pathological conditions with which it is most frequently associated are a stenosis of the coronary arteries and a fatty degeneration of the heart, which arises from that condition of the vessels. The stenosis may exist in the course of the vessels, and is then frequently calcareous, or it may occur at their orifices, when it may or may not be calcareous. In any case the condition upon which the arterial stenosis depends is atheroma. The atheroma of the coronary arteries is often conjoined with atheroma of the aorta itself, and not infrequently with organic disease of the segments of the aortic valve.

Angina pectoris is a frequent cause of sudden death, and at the autopsy all the cavities of the heart are found over-distended with blood. The condition is, therefore, one of cardiac paralysis, and an important corroboration of this view is afforded by the fact that those drugs which lower arterial tone (e.g. amyl nitrite and nitroglycerine) are particularly serviceable in combating the condition.

Brown atrophy is a pigmentary degenerative change to which sufficient reference has already been made (p. 26).

Cloudy swelling is of frequent occurrence in the heart muscle of persons who have died as the result of a toxic disease which has been accompanied by fever. It shows itself by a loss of that deep colour that is characteristic of the normal myocardium and its replacement by a more or less turbid colour of a lighter shade. Microscopically the muscle fibres are found to have lost their striation in large measure and to have become granular.

The **lardaceous** and **hyaline** changes are met with in the myocardium as elsewhere in the body. They do not, however, lead to any macroscopic changes in the appearance of the organ. For this reason they are said to be of infrequent occurrence in this organ, but an insufficient number of cases has been examined for us to speak upon the point with certainty.

Chronic fibrosis, or, as it is often termed, fibroid degeneration, of the heart is a condition which is somewhat rare, but nevertheless forms about ½ to 1 per cent. of the causes of death in the autopsies made at the London hospitals. It is characterised by the replacement of portions of the myocardium by masses of dense fibrous tissue similar to that found in a scar. The masses of fibrous tissue are of very different sizes in different cases. Sometimes they are only as large as a pea, but sometimes there is a mass as large as a five-shilling piece, or even larger, at one spot. Thus the entire lower third of the left ventricle may be converted into a mass of fibrous tissue. As a rule there are large numbers of these fibrous foci scattered throughout the muscle of both ventricles, so that a fibroid heart with its irregularly disposed and irregularly shaped masses of white fibrous tissue comes to resemble in appearance very closely, macroscopically, a heart the subject of 'tabby-cat striation.'

Under the microscope it is seen that the fibrous-tissue overgrowth is present in many situations which seem to consist, to the naked eye, of perfectly normal myocardium. There is, in fact, a general excess of the tissue, and it is not only present in the inter-muscular septa, but also replaces smaller or larger tracts of the myocardium itself. The connective tissue, too, is of an extremely chronic type, and the number of cells present is small, while the nuclei of the cells are shrivelled and angular in shape and stain deeply.

The presence of the excessive amount of fibrous tissue is accompanied by a disappearance of a corresponding amount of muscle substance, and at the edges of a mass of fibrous tissue it is easy to see that the muscle bundles are undergoing atrophy. Whether this atrophy is to be regarded as a secondary or as a primary change, is a question to which no sure answer can be given. There is a general tendency to believe that the fibroid change is, fundamentally, syphilitic, and since we know that syphilis sometimes occurs in the heart muscle in a form which is nothing more than granulation tissue, it is possible that the fibrous tissue present in the fibroid heart is really of the nature of scar tissue. But, on the other hand, the fibroid change is hardly ever met with in any but a well-formed stage, so that it has the greatest resemblance in this as in many other points to the chronic fibroses.

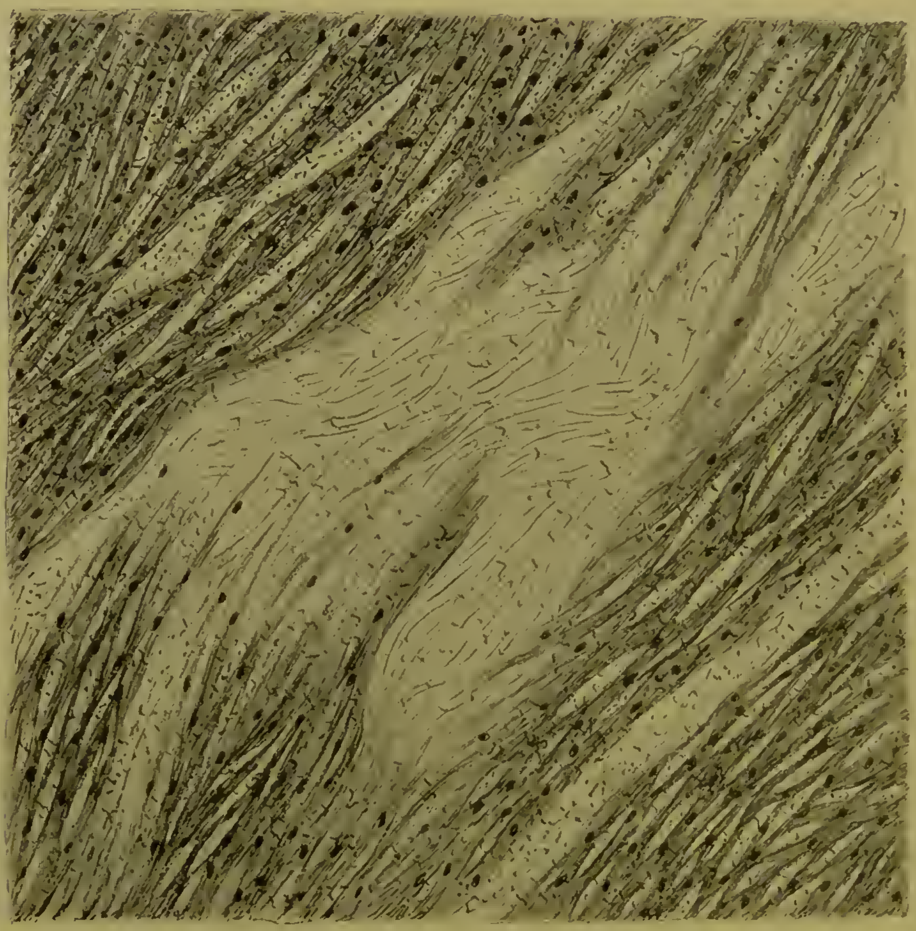


Fig. 69.—Section of Myocardium showing Chronic Fibrosis. × 420.

A large irregular patch of dense fibrous tissue lies in the midst of muscle fibres, and there are smaller foci situated elsewhere between individual muscle bundles. Linear or angular nuclei of adult connective-tissue cells are seen over the entire section.

We have already referred to the formation of acute aneurysms of the heart in association with inflammatory, and particularly with suppurative, conditions. Yet another form of cardiac aneurysm is known. It is the chronic form and arises in connection with the fibroid change. Most commonly the condition amounts to little more than a localised bulging of a portion of the ventricular wall, but sometimes a more or less definite aneurysmal sac is formed at a region over which the ventricular wall has become replaced by fibrous tissue. As might be expected, such aneurysmal dilatations of the heart are met with almost exclusively in the left ventricle, and then generally about the apex.

(3) **Changes occurring in the heart as a composite muscular organ.**—As the result of the numerous influences to which it is exposed, the heart is liable to manifest great divergence from the normal in size and shape. These changes may concern the auricles or the ventricles, either on one side of the heart or on both.

The actual change that is manifested depends upon the cause that brings it about. For the heart, being a muscular organ, is subject to the laws governing muscle, and does not undergo a spontaneous modification in size apart from that coincident with the growth of the individual.

The essential factors which determine the size of the heart are the state of its nutrition and the amount of work it is called upon to perform. The same factors determine the condition in each of the cavities of the heart, so that if we find a given cavity dilated or its wall hypertrophied, it is only necessary to look for the condition which brings one or other of these two essential factors into play.

Speaking broadly, we may say that any obstruction at one of the orifices of the heart is followed by an hypertrophy of the muscular wall of the cavity which lies immediately behind it. Thus, if there is a stenosis at the aortic orifice, the left ventricle becomes hypertrophied; if there is a stenosis at the mitral orifice, the left auricle becomes hypertrophied. The exact converse is also true. For if the foramen ovale remains patent and allows of the passage of blood from the right auricle to the left, the right ventricle is called upon to do less work, and is therefore found to be of smaller dimensions and to have a thinner wall than normal. So, too, when the mitral orifice is greatly stenosed, it is not uncommon to find that the left ventricle is smaller than normal. Nevertheless this point is not observed with as much constancy as the others that have been mentioned.

On the right side of the heart the walls are thinner than on the left, and as a result the effects of an equal degree of stenosis are not the same on the two sides of the organ. For on the right side there is a much greater tendency for hypertrophy to be slight or wanting and for dilatation to be conspicuous. There are other causes for this difference to which attention will be drawn presently.

In the very large majority of cases hypertrophy of the muscular wall of a cavity of the heart is accompanied by an increase in the dimensions of the cavity itself. We cannot here enter into a discussion of the causes of the dilatation, but it may be shortly said that it depends upon the fact that the cavity is called upon to contain a larger amount of blood than normal. The more muscular the wall of the cavity is, the less the tendency for the occurrence of dilatation, and *vice versâ*. Hence we meet with dilatation more frequently in the auricles than in the ventricles, and in the right ventricle than in the left.

The state of nutrition of the myocardium is a most important factor in determining whether the effects of a stenosis shall be in the direction of dilatation or of hypertrophy. One can go further, and say that whenever nutrition fails in a heart that is undergoing hypertrophy, that condition immediately ceases and gives place to dilatation. The latter point is one of the greatest importance, for it indicates that the normal end of an hypertrophy of the heart is in an increasing dilatation, and, as a matter of fact, we have ample clinical and pathological evidence that this reversal of states is constantly going on. Apart from accident, it is the natural termination to every form of cardiac disease.

The dilatations and hypertrophies of the various cavities of the heart cause the organ to assume many different shapes. In cases of aortic stenosis, and the same may be said of aortic regurgitation, we find an enormously hypertrophied and considerably dilated left ventricle. Nor does the ventricular change depend upon an increase of work thrown upon the left ventricle at the aortic orifice alone. For a very considerable hypertrophy, here unaccompanied by dilatation of any extent, occurs when the increase of work is imposed in the peripheral portions of the arterial system, as it is in the condition of arterio-sclerosis present in cases of chronic renal fibrosis. In cases of mitral stenosis it is the left auricle that is affected, and here, although we meet with a certain amount of hypertrophy, it is the dilatation of the cavity which is generally most striking. On the right side of the heart dilatation of the cavities is frequently considerable. Thus it occurs in connection with the ventricle in all cases in which there is an impediment to the progress of the blood through the lungs, and whenever the tricuspid valve fails to close satisfactorily, the obstacle at its orifice leads to a dilatation of the right auricle that can at times only be described as enormous.

It will readily be seen from the foregoing considerations that the effects of any lesion in the vascular system are gradually thrown backwards from cavity to cavity. Supposing, for example, that a condition of arterio-sclerosis is established, the first effect is an hypertrophy of the left ventricle. This continues so long as the nutrition of the muscle composing the wall of this cavity remains good. But so soon as it fails, the cavity dilates, and the auriculo-ventricular ring dilating with it, mitral regurgitation is set up. An obstacle is now set in the way of the free entry of the blood from the lungs and the left auricle, with the result that the auricle dilates and the lungs become congested. An obstacle is presented, too, to the opening of the pulmonary valve, and an increased amount of work is thrown upon the right ventricle. The right ventricle consequently hypertrophies in some degree, but the nutrition of the myocardium generally being impaired by the difficulties which the left heart has been experiencing, the amount of hypertrophy is small and the degree of dilatation proportionately large. Ultimately the dilatation of the right ventricle becomes so great that the stretching of the auriculo-ventricular fibrous ring, and the distance between the bases of the musculi papillares, become so considerable as to be incompatible with the proper closing of the tricuspid valve during systole. As a result an obstacle is presented to the entry of the blood from the right auricle and the entire venous system, the pressures therein are raised, and the cavities themselves become dilated.

In connection with the statement that increase of work thrown upon the heart is followed by hypertrophy, an important exception must be made. It is essential that the excess of work that is imposed should not be beyond the powers of the organ to cope with. If it be so great that the heart cannot cope with it at all (e.g. if a ligature be pulled tight around the aorta), the heart simply stops work and dilates passively until the venous and pulmonary blood pressures are no longer able to expand the cavities any further. If the obstacle is not so great as this, but is nevertheless beyond the powers of the heart, it does not instantaneously cease work as in the other case, but it goes on working, and, although dilating more and more with each successive systole, continues to work until the dilatation has become so great that the amount of blood which the ventricle is called upon to force into the aorta unites with the initial obstacle itself to form an insuperable obstacle. When this point is reached the organ stops pulsating as before. Many of the cases of death by syncope are to be explained in this way; only one has to add that the degree of obstruction needs to be less owing to the fact that the nutrition of the heart has been profoundly modified, probably by some other cause (e.g. fatty degeneration, poisoning by the toxin of diphtheria, &c.).

(4) **New-growths.**—The new-growths of the myocardium are very few, and are almost invariably secondary. Primary growths are almost always non-malignant, and are generally either small fibromata or lipomata. Secondary nodules have been found of both carcinoma and sarcoma, and of these carcinoma is the commoner, owing to the proximity of the organ to the breast and the frequency with which this gland is the seat of carcinoma.

(4) CONGENITAL MALFORMATIONS OF THE HEART

It will not be necessary for us to enter at any length into a consideration of the congenital malformations of the heart, partly because they are of comparatively rare occurrence, and partly because they possess rather an embryological than a pathological interest. Nevertheless they are, in a large number of cases, accompanied by a train of symptoms which differs in many respects from that which accompanies acquired heart disease, and therefore they must receive some notice.

Congenital malformations of so slight a degree that they are only discovered accidentally at the autopsy are not so very uncommon. It is a little difficult to decide which form of malformation of this kind is the most frequently met with. Some authors maintain that a slight degree of pulmonary stenosis is the commonest of the congenital malformations, and if we regard those conditions that are strictly congenital probably this view is correct. But if the processes concerned in the closure of the foramen ovale are included in the category of congenital conditions, there is no doubt that some degree of failure to obliterate completely the foramen ovale is the commonest. The condition is then spoken of as patency of the foramen.

The degree of patency of a foramen ovale may vary between a condition in which the deficiency does not interfere in the slightest degree with the welfare of the patient to a condition in which the most profound evidences of congenital heart disease are present. It does not follow that in the former case the unobliterated portion of the foramen is of extremely small size. On the contrary, there may be a gap sufficiently large to admit the tip of the little finger. But then the opening is always imbricated, so that it is impossible for blood to pass from one auricle to the other during life owing to the existence of pressures on both sides of the septum that are approximately equal and opposite. Whenever the communication between the two auricles is other than only potential or extremely minute, symptoms of congenital heart disease are produced.

Far less common than deficiency of the septum between the two auricles is a deficiency between the two ventricles. When this condition occurs it is generally found to consist in a deficiency of the septum ventriculorum at that portion which is termed the 'undefended spot.' This spot is at the base of the septum, close to the origin of the aorta and the pulmonary artery. It normally consists of little more than thin but dense connective tissue, and is the last portion of the septum to be formed in the development of the heart. Congenital malformation of the heart of this kind is almost always accompanied by symptoms.

Other malformations are known to occur. Such are the presence of two cusps instead of three in the tricuspid or aortic valve, the presence of a third, usually very small, cusp in the composition of the mitral valve, &c.; but these modifications do not lead to any morbid symptoms, and therefore do not call for our especial attention here.

In the case of a malformation of the heart of any extent, it is always possible to say that congenital heart disease exists, although it is almost always impossible to say what condition it is that is actually present. Nor is it possible to predict with safety the degree of malformation that is present. For the most extravagant symptoms may exist in a case in which what we should consider to be a relatively minor degree of malformation is found after death, and, on the other hand, a degree of patency of the foramen ovale may be present, so great that the right ventricle is less than half its normal size, and yet the person may have lived to old age without having given evidence of any cardiac disease at all.

The symptoms which, when present, lead to the formation of a diagnosis of congenital heart disease are chiefly three, viz. cyanosis, clubbing of the fingers with incurving of the nails, and breathlessness upon exertion. The cyanosis varies from so slight a degree that it is only recognised after careful examination to a dull leaden blueness of the entire surface of the body, most marked, however, over the face, hands, and feet. Clubbing of the fingers is usually present in a marked degree, and undoubtedly depends in part upon an increase in the amount of the fibrous tissue present over the terminal phalanges. Probably this overgrowth depends upon the venous congestion, and has analogies with the fibrous-tissue overgrowth which occurs in the kidney, the liver, and, to a less extent, in the spleen, in cases in which acquired heart disease has led to a general congestion of the entire venous system.

SECTION III

THE BLOOD-VESSELS AND LYMPHATIC VESSELS

It will be convenient if we divide this section according to the type of vessel affected. We shall therefore consider (1) the arteries, (2) the veins, (3) the capillaries, and (4) the lymphatic channels.

(1) THE ARTERIES

In some degree all the arteries of the body are affected by pathological processes alike, but there is a very great difference in the frequency with which the different systems of artery are involved. Thus it is exceedingly common for atheroma to occur in the aorta, it is not uncommon in the small systemic arteries, but it is excessively rare in any of the branches of the pulmonary artery, whether large or small. Similarly the modification known as arterio-sclerosis is one which affects the systemic arterioles alone.

(1) **Hypoplasia and atrophy.**—These conditions are of frequent occurrence in the case of the arteries. They accompany in most cases the same modifications of the parts which they supply with blood. Thus, when the lower limb on one side is smaller than its fellow, as the result of an attack of acute anterior poliomyelitis in childhood, the femoral artery and its branches share in the general ill development. So, too, the femoral artery undergoes atrophy when the leg has been amputated for any cause. In this case the atrophy is nothing more than an atrophy from disuse.

When an artery undergoes atrophy, not only do its walls become thinner, but its lumen becomes smaller owing to the diminished amount of blood which it is called upon to convey. In cases of hypoplasia the same is true in some measure, but it is commoner for the thinness of the walls to attract more attention than the actual diminution of the vessel's calibre.

Atrophy of arteries is almost always associated with some pathological condition of the tissues supplied by the vessel that is easily recognised, but this is not so constantly the case with hypoplasia. It is common, in particular, to find in anæmic women that the aorta is hypoplastic, but there is no evidence that the tissues of the body have been supplied with an insufficient amount of blood. Beyond the fact that the hypoplasia of the aorta is frequently met with in association with anæmia of young women, nothing is known concerning the pathology of the condition.

(2) **Degenerations.**—The arteries are very prone to degenerations of different kinds, but there is much difference between the larger and the smaller arteries in the matter of the particular kinds of degenerative change to which they are liable. Some of these degenerations are true degenerations from first to last. Such, for example, is the fatty degeneration which often affects the intima of the aorta in persons over middle age. Others are preceded by a condition in which there is an overgrowth of some one element entering into the composition of the vessel-wall. Such is arterio-sclerosis, and probably the same is true in many cases of atheroma. Whether the walls of the arteries are the subject of infiltrations it is difficult to say. In the cases of the lardaceous change and the hyaline change, it is, as has already been said, impossible to say with certainty whether the condition is one of a true degeneration or of an infiltration.

Atheroma.—Atheroma is the most important of all the pathological changes undergone by the arteries. This is so, not only by reason of the immediate alterations which it induces in the walls of the affected vessels themselves, but also because of the numerous and serious alterations of which atheroma is merely the precursor.

Although it cannot be said that atheroma generally is a syphilitic change, there is no doubt that syphilis is an important factor in its causation. Nevertheless there is reason to believe that hard muscular work, by throwing increased strain upon the heart, is a cause of the degeneration, apart from syphilis. The soft form of atheroma is, in all probability, always syphilitic.

Though atheroma is by far the commonest affection of arteries, so common, indeed, that some evidences of its existence are to be found in more than half the bodies of middle-aged persons that are examined in the *post-mortem* room, it is far less often recognised as such than might be expected. The reason of this is not far to seek. For the change is a degenerative one and chronic, and it is especially under such conditions that there is a liability to the local deposition of calcium salts. Hence the actual modification of the vessel-wall that is present in the majority of cases consists in the replacement of portions of the wall by more or less extensive and firm calcareous plates. These plates mark the sites at which the atheromatous change formerly existed, but they do not constitute it. Unfortunately it is customary to speak loosely of such a calcification of the aorta as 'atheroma.'

Although the aorta is not the only artery which is liable to be affected by atheroma, it is far the commonest seat for the change. Usually it is the arch that is affected, but the entire vessel may be extensively diseased. Even then the greatest amount of disease is probably in the arch. Another common situation for the change is the abdominal aorta immediately above the bifurcation, and we sometimes find the greatest evidences of disease in this situation.

When the aorta is extensively diseased, it is usual for the large arteries to be similarly affected. But here the condition is less calcareous than it is in the aorta, so that we are able to select from a single case portions of vessels showing various stages in the change. Frequently, however, the only difference between the foci of disease in the aorta and in the large arteries is one of extent, the condition being equally chronic throughout. In such cases the calcareous change may extend to arteries as small as the radial.

In somewhat rare instances atheroma is found to affect the arteries extensively and to be present in the stage that precedes calcification. When such a condition obtains it is sometimes said that the vessels are the seat of 'soft' atheroma. In such cases the amount of atheroma present is commonly greater than it is under any other condition.

Atheroma may affect the arteries quite irregularly, or it may be arranged more or less circularly around them. In either case, and also whether the condition is soft or calcareous, it causes a projection into, and proportionately diminishes, the lumen of the vessel. When it has become the seat of calcification there is an absence of a covering layer of endothelium, and, as a result, there frequently takes place a deposition of colourless or of red thrombus over or around the focus. This is not the case when the atheroma is soft.

Soft atheroma is easily examined microscopically. In all instances in which the condition is well marked, there is a considerable increase in the thickness of the intima and media over a smaller or greater portion of the vessel-wall. This increase is generally somewhat irregular, although the surface towards the lumen of the vessel is smooth. The thickened coats consist in their deeper parts of a number of layers of a homogeneous but slightly granular material, which are arranged in a direction parallel with that of the vessel-wall. The material shows here and there nuclei of the connective-tissue type which, as a rule, stain but poorly. In addition the layers of which the material consists manifest a certain number of narrow clefts which seem to lie between the fibres and give evidence of the little cohesion which exists between the component layers. The granular appearance vividly recalls that of a tubercle undergoing caseation. In such a case it is sometimes possible to see the elastic lamina, but as a rule it is wanting at the actual seat of the atheromatous change.

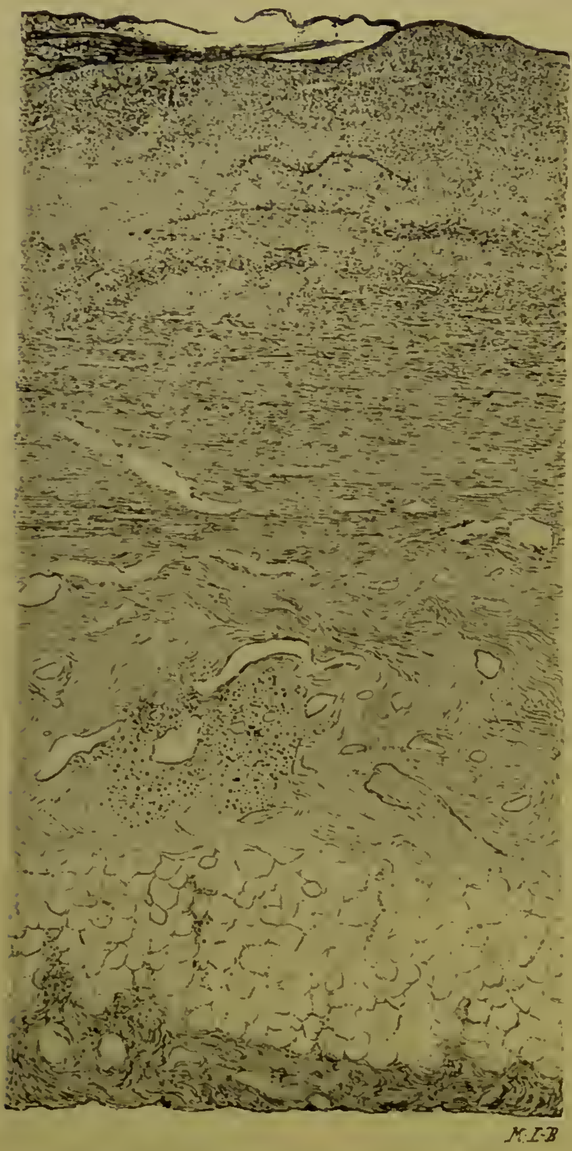


Fig. 70.—Soft Atheroma of Femoral Artery. × 40.

The intima and media constitute the upper three quarters of the figure and are enormously increased in thickness compared with the adventitia (lower fourth). The intima, irregularly and faintly distinguishable from the media, is infiltrated with leucocytes. The media is divisible into two parts, the upper half consisting of numerous parallel layers running from right to left and the lower half composed of fibres more irregularly arranged and carrying most of the vasa vasorum. The upper half is composed of an almost structureless granular material, the lower consists of fairly recognisable fibrous and elastic tissue with a localised accumulation of leucocytes. The fenestrated membrane of Henle has disappeared.

Although the appearances of an atheromatous patch are, in the vast majority of cases, those which have been described above, it is probable that they do not represent the earliest changes in atheroma. It is generally taught that the earliest change consists in a proliferation of the cells constituting the deeper layers of the intima, those, that is, which lie in immediate contact with the elastic lamina. The accumulation of these cells produces a projection into the lumen of the vessel, and since the cells are not nourished by the vasa vasorum, those furthest away from the lumen die and undergo degenerative changes. It is further taught that these degenerative changes are accompanied by a chronic, but true, inflammation, so that the internal portion of the vessel becomes replaced by a fibrous form of granulation tissue, which, from its character, readily undergoes degeneration. It follows, from what has just been said, that the arterial changes in atheroma are regarded, by some authors, as a special variety of arteritis.

It must be confessed, however, that the changes which have been described in the last paragraph are very difficult to make out. And it is at least open to question whether the changes which occur in true syphilitic endarteritis (endarteritis obliterans), and which are undoubtedly of a chronic inflammatory nature, have not, owing to the very fact that caseation is a constant feature of both lesions, been confused with those which occur in atheroma. Such an explanation is the more plausible in that the soft form of atheroma is, as has already been remarked, closely associated with syphilis.

It does not always happen that a patch of atheroma either forms a simple projection into the lumen of the vessel or becomes the seat of calcification. Sometimes the degenerated material becomes sufficiently softened, and involves so considerable a proportion of the entire atheromatous mass that caseation extends to the layer of endothelial cells which overlies the mass and forms the lining wall of the vessel itself. Under these circumstances the softened mass will probably discharge itself into the lumen of the vessel, with the result that a weakened spot is formed in the vessel-wall. The floor of such a weakened spot is rough and crumbling, the edges often undermined for some distance, and the 'atheromatous ulcer,' which is thereby constituted, may extend deeply into the middle coat of the vessel.

Calcareous deposition may take place in the floor of an atheromatous ulcer subsequent to its formation, and if this occurs the event may be regarded as most fortunate. For it is far more common to find that the formation of an atheromatous ulcer is but the prelude of one of the most formidable affections of the arteries, viz. an aneurysm. To the subject of aneurysms in general we shall direct our attention later.

When atheroma is so extensive that it involves even vessels no larger than the radial artery, and when, in addition, it is accompanied by a great degree of calcification, it is frequently said to constitute the condition of **arteritis deformans.** The radial artery, in such cases, is tortuous and completely incompressible, while the brachial at the bend of the elbow may give the impression of a metal tube to the finger. Arteritis deformans is rarely met with except in the aged, but it may occur in younger persons who are the subjects of chronic renal disease. Under the latter circumstances it is probable that the calcified condition supervenes upon arterio-sclerosis. In these cases, too, the calcareous condition may supervene in a comparatively short space of time. Thus, in a case which came under the author's notice, the patient was a young woman aged twenty-eight, who was in hospital in February with acute renal disease, characterised by the usual signs and symptoms, and whose arteries were quite soft. She left hospital much improved in health in March, but was re-admitted and died in the following November. At the autopsy the radial artery was found to have become so greatly calcified during the interval that when the vessel was dissected out for its entire length, it was possible to hold it by the lower end and show the whole length of the artery standing vertically upwards by virtue of its own rigidity.

The most important result of arteritis deformans is shown in its effects upon the nutrition of the tissues which are supplied with blood by the modified arteries, i.e. in the production of gangrene. Senile gangrene, in particular, is dependent upon this arterial change, although other factors may conjoin in its causation. The actual death of the tissues occurs by way of the thrombosis that takes place in the altered vessels. The fact that the collateral branches are themselves the seat of calcareous changes militates forcibly against the establishment of a collateral circulation, while the feebleness of the heart which is present in old age further contributes to the final result.

When the degree of obstruction which is interposed in the way of the circulation is not sufficient to lead to gangrene, it not infrequently leads to the occurrence of fatty degeneration of the tissue elements which draw their blood supply from the calcareous vessels. The best example of this statement is found in the case of calcification of the coronary arteries of the heart. Reference has already been made to this point in connection with the disease known as angina pectoris (p. 286).

Aneurysm.—Strictly speaking an aneurysm is nothing more than a widening of an artery, but since the widening takes different forms it has become customary to divide aneurysms into certain varieties. These are (1) fusiform, (2) saccular, (3) dissecting, and (4) traumatic. A fifth variety (cirsoid) is sometimes included, but this is rather a special arrangement of newly formed arteries than an actual dilatation of a portion of one that is already in existence; it therefore has closer relations with the new growths than with the aneurysms properly so called.

A **fusiform aneurysm** is merely a local dilatation of a portion of an artery. Such aneurysms are only found to occur in the aorta, and all the coats of the vessel are concerned in their formation. They are of little practical importance.

The **saccular aneurysm** is the most important of all the varieties, not only by reason of its frequent occurrence, but also because of the effects it has upon the tissues in its neighbourhood.

In the saccular aneurysm all the coats of the normal vessel are not represented. There is a complete absence of the intima, and, generally, a considerable portion of the thickness of the middle coat is wanting also. These points are generally recognisable without difficulty, particularly in the case of small aneurysms of rapid formation. The actual composition of the wall of the aneurysmal sac itself is not so easy to determine. There is no doubt that the adventitia of the vessel is represented in it, but the changes that are undergone by the tissues in the immediate neighbourhood of the sac are such, that large portions of them, altered out of recognition, are incorporated with the adventitia in the formation of the sac. These changes in the neighbouring tissues resolve themselves into the combined effects of a pressure atrophy that is induced by the enlarging sac, and a new formation of inflammatory fibrous tissue due to the irritant action exerted by the sac. In the large majority of cases the atrophic changes outweigh the conservative, so that the wall of a saccular aneurysm is usually much thinner than the wall of the vessel from which it springs. For the same reason we find that not only soft tissues, but even bone, are gradually absorbed in front of an advancing aneurysm. (Cf. fig. 5.)

Saccular aneurysms may be almost of any size, but the size depends, as might be expected, principally upon the size of the vessel upon which they are situated. Thus an aneurysm of the ascending part of the arch of the aorta may be as large as the two clenched fists of a man, while an aneurysm upon the middle cerebral artery rarely reaches to the size of a pea. Nevertheless we sometimes find at an autopsy that an aneurysm of the aorta has proved fatal before it has become larger than a pea; such small aneurysms are most liable to be formed in the intra-pericardial portion of the ascending arch, and to rupture, therefore, into the pericardial sac.

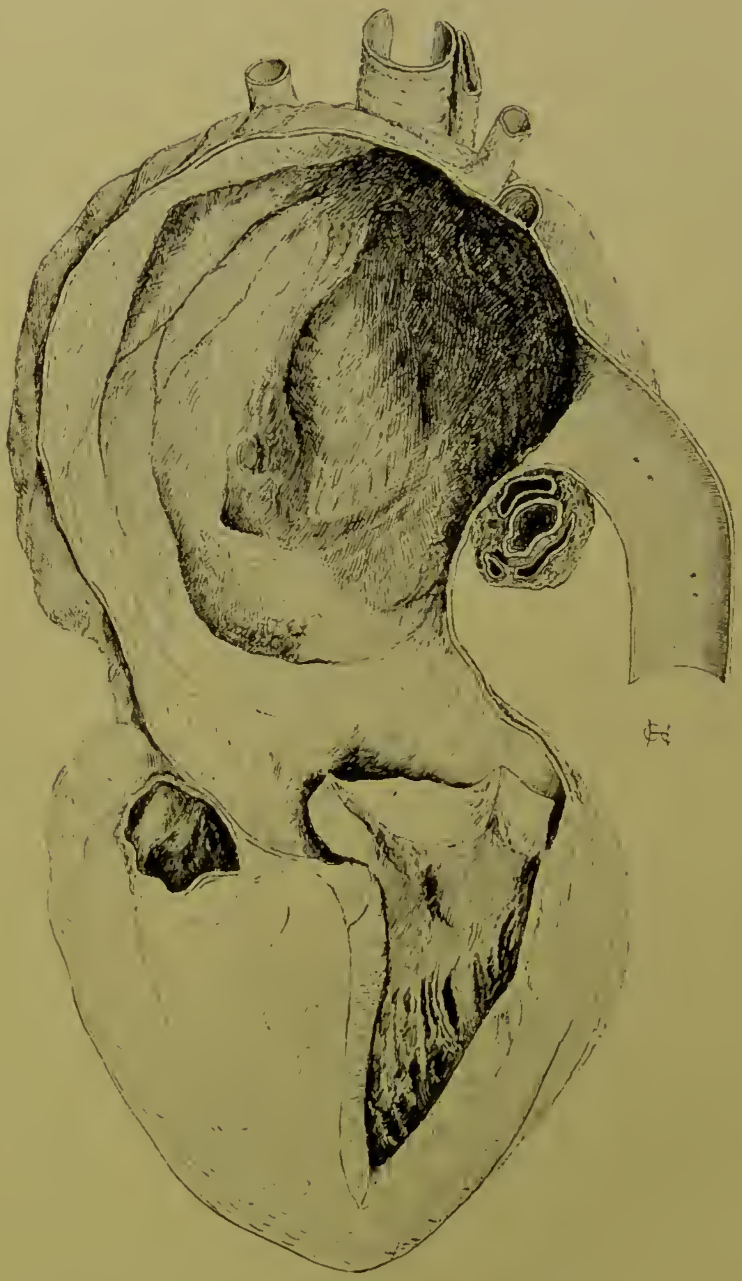


Fig. 71.—Saccular Aneurysm of Arch of Aorta. × $\frac{2}{3}$.

A short distance above the aortic orifice the aorta is expanded into the aneurysmal sac. Note that the cusps of the aortic valve are not involved, and that the heart is not hypertrophied.

Saccular aneurysms are rarely completely saccular. Most frequently they are situated upon a portion of an artery that is more or less extensively diseased. Hence beyond the actual confines of the sac, the vessel is dilated so as to form a fusiform aneurysm. This is often well seen in the case of saccular aneurysm of the transverse portion of the arch of the aorta, for the commencements of the innominate, the left carotid, and the left subclavian arteries are, under such circumstances, almost always in a condition of fusiform aneurysm.

The **dissecting aneurysm** is not very often seen, but when it is met with the striking characters of the symptoms by which it is accompanied, and the peculiar features of the anatomical lesion found, are such that the condition can hardly be mistaken. For the change consists in a separation of the walls of the vessel in the substance of the media and an effusion of blood into the space thus formed.

Dissecting aneurysm is a condition that is hardly ever found in the case of other arteries than the aorta, though it may affect the large branches of the aorta such as the common iliacs, secondarily. On carefully examining a case, it will almost invariably be found that there is a small rent in the intima at some point in the arch of the aorta, most generally the intra-pericardial portion of the ascending arch. This rent is obviously at the situation of an atheromatous ulcer. Opposite, or nearly opposite, to this rent in the intima is a rent in the adventitia, while between the intima and the adventitia is a mass of blood clot that extends throughout the entire length of the aorta and perhaps involves a part of the middle coats of the principal branches as well. The symptoms that accompany the formation of a dissecting aneurysm suggest strongly the method of its production. For there occurs in a person of adult age, almost always a male, at a period when he appears to be in perfect health, a sudden agonising and tearing pain in the thorax ; after a short time he becomes somewhat easier, but, suddenly and without warning, perhaps ten or twelve hours after the first onset of pain, the patient cries out and drops back dead. It cannot be doubted that the first paroxysm of pain accompanies the rent into the intima and the separation of the middle coat of the vessel, that the period of comparative repose corresponds to the period which elapses between the rent in the intima and that of the adventitia, and that the final pang is due to the rupture of the adventitia and the outpouring of blood into the pericardial sac or the pleural cavity, as the case may be.

Although there is no doubt that the formation of the initial rent into the vessel is occasioned by the existence of a patch of atheroma, the pathological condition of the middle coat of the vessel which allows of its separation by the small force that can be exerted by the aortic blood pressure (and no other force is available) is quite unknown. Probably, however, it consists in the existence of a fatty degeneration, or in some change that is closely akin thereto.

A so-called **traumatic aneurysm** is not a sac formed by all or a part of the wall of the artery, but is of an entirely artificial formation. It results from the effects of a rupture of an artery, and for this reason is particularly liable to be found in the case of arteries that are especially exposed to injury (e.g. the popliteal). The method of its formation is as follows. In consequence of the lesion in the arterial walls a certain amount of blood is effused into the surrounding tissues. This effused blood coagulates, and by contraction of the fibrin thus produced the mass of effused blood and tissue elements comes to possess a more or less well-defined globular shape. But the coagulation does not occur in the centre of the mass, so that the circulation continues between the two ends of the ruptured vessel by way of the space which lies between them. Hence it appears as if the blood-containing sac were a portion of the vessel as much as it is in the case of a true saccular aneurysm. It is clear, however, that the methods of formation of the two types of aneurysm are totally different. For this reason a traumatic aneurysm is sometimes spoken of as a *false* aneurysm.

In placing the subject of aneurysm in juxtaposition with that of atheroma, the fundamental fact will have been brought out that atheroma is the most common cause of aneurysm. It must not be supposed, however, that atheroma is the only cause. We may probably take it for granted that atheroma has been an antecedent of all aneurysms seated on large arteries, and in particular of all aneurysms of the aorta. But we find aneurysms seated upon small vessels, and in the case of these atheroma cannot be inculpated with the same degree of certainty.

The most important form of aneurysm seated upon small arteries is that which is found to occur upon the cerebral vessels of persons affected with chronic renal fibrosis. As a cause of death there is no doubt that these small aneurysms are far more important than aneurysms even of the aorta. For it is owing to their rupture that the condition of cerebral hæmorrhage or apoplexy is brought about. Frequently it is possible, with a little care, to find several localised swellings the size of a small pea or less upon the branches of the middle cerebral artery, and similar formations may be found upon others of the cranial vessels. Under such circumstances we may find marked evidences of atheroma in the arteries, not only of the body generally, but also of the brain. It cannot be asserted, therefore, that these small aneurysms have certainly not originated from the previous occurrence of atheroma. But, in spite of this fact, there is a large amount of evidence that similar aneurysms may result from the lodgment of an embolus. As to the actual mode in which the embolus leads to the formation of the aneurysm, and as to whether the aneurysm is formed in front of, at, or behind the seat of obstruction, we are at present without full information. In cases, however, in which the embolus has been septic, there is no doubt that the aneurysm is of acute formation, and that it is produced immediately around the embolus.

Another important cause of aneurysms on small arteries is tuberculosis. Such aneurysms are sometimes to be found in the vomicæ present in cases of pulmonary tuberculosis, and even if they are not to be found with extreme frequency there is little doubt that their rupture is accountable for one form of hæmoptysis.

The effects of aneurysms are chiefly mechanical. It is clear that a sac the size of the clenched fist or greater cannot be present in the region normally occupied by the arch of the aorta without compressing and displacing the other structures in the same region. Thus, to mention only one effect, when the aneurysm concerns the transverse portion of the arch, the recurrent laryngeal nerve must be stretched, and the result will be that laryngeal symptoms will be produced varying from spasm due to irritation to paralysis the effect of complete compression.

Another important result of the pressure exerted by aneurysm is atrophy. This is seen very well in the case of an aortic aneurysm affecting the ascending portion of the arch. For the sternum and the costal cartilages in the region of the third space on the right side are, in time, completely absorbed, and the aneurysmal sac presents as a soft pulsating mass covered only by a layer of atrophied skin. When, as in the case of an aneurysm affecting the descending aorta, the pressure of the sac is exerted upon nerves that carry sensation, not only is it accompanied by a considerable necrosis of bone, but also by excruciating pain that follows the course of the nerves affected.

Owing to the thinning of the vessel-wall where the aneurysm is situated, and the pressure atrophy to which it leads, rupture of the sac is a common termination of an aneurysm. Sometimes rupture occurs before the sac has attained to any considerable size, and in these instances the rupture is due to some sudden effort which momentarily increases the general blood pressure.

Rupture is then accompanied by the outpouring of a large quantity of blood, and is usually directly fatal. But when the sac has reached to some size the definitive fatal rupture is often preceded by a period during which slight oozing takes place; such oozing may go on for days or even weeks. The spot at which an aneurysm ruptures is determined by a variety of considerations into which we cannot enter here. It may be said, however, that aneurysm of the ascending part of the arch of the aorta most commonly ruptures externally, while aneurysm of the transverse arch ruptures into the trachea or one of the bronchi, and aneurysm of the descending aorta ruptures into the left pleural cavity. Nevertheless it must be remembered that, although rupture is the usual mode of termination of an aneurysm, it is not the only one. In fortunate cases the cavity becomes filled with clot deposited from the blood, and the sac becomes converted into a solid tumour, and in other cases in which death occurs it is caused, not by rupture, but by some intercurrent disease, probably of the lungs, to which the paralyses induced by the pressure in many instances directly tend.

Upon the heart itself an aneurysm, as such, has no effect. It simply increases by so much the capacity of the vascular system, and does not throw any extra work upon the organ. Of course it is not uncommon to meet with conditions in which an aneurysm of the aorta coincides with an atheromatous state of the aortic semilunar cusps. Under such circumstances it is to be expected that there will be hypertrophy and dilatation of the left ventricle. But the ventricular change depends upon the aortic regurgitation or stenosis that is produced thereby, and not upon the presence of the aneurysm.

(3) **Arterio-sclerosis.** — Closely related to the degenerative processes which occur in arteries is one which cannot be said to be distinctly degenerative, but which often precedes the onset of degeneration. It consists in the presence of an increased thickness of the middle coat of the smaller arterioles. This thickening is frequently so considerable that it can easily be recognised by the naked eye, and it gives to the affected arteries a greatly increased rigidity. The change is one which occurs generally throughout the body, and is met with in association with chronic fibrosis of the kidney (red granular kidney).

The arterial change itself is in part one of hypertrophy of the muscular elements of the middle coat and in part one of fibrosis. Its beginnings are never seen or at least recognised, and although we cannot doubt that the arterial condition bears some close relation to the great hypertrophy of the left ventricular wall, which also occurs in chronic renal fibrosis, it is impossible to say whether the cardiac modification is the result of the arterial change (and this is probably the case) or whether they are both of them coincident evidences of one general morbid change affecting the entire system supplied by the left ventricle, or whether, again, the cardiac condition precedes in point of time the arterial. Each of these views has had its supporters.

Arterio-sclerosis frequently co-exists with atheroma of the aorta and other large vessels, and in these cases there is generally a considerable deposition of calcium salts in the atheromatous patches. The arterio-sclerotic change may itself be antecedent to the onset of atheroma with calcification, but it is doubtful whether this is so common a change as is generally supposed.

It is only necessary here to recall to mind the fact that the middle coats of the smaller arterioles are also the seat of the lardaceous change. Sufficient has been said on this point elsewhere.

(4) **Arteritis.**—It is a matter of doubt how far the arteries are liable to true inflammation. By many authors the atheromatous change is included under the category of the inflammations. For reasons that will have appeared they have been included above with the degenerations, so that we shall consider in the present class only those varieties of arterial change which come, unequivocally, among the inflammations.

The simplest form of arteritis is that which arises as the result of the extension to an artery of an inflammatory process which has commenced in its neighbourhood, or which has been induced within the vessel itself owing to the local lodgment of an embolus. In either of these cases the ordinary phenomena of inflammation manifest themselves in the tissues constituting the wall of the vessel, the vascular changes occurring in connection with the vasa vasorum. In consequence of the modification of the endothelium which accompanies the existence of the inflammation of the main part of the arterial wall, a thrombosis is set up in the lumen of the affected vessel. The ultimate fate of the thrombus and of the vessel itself will depend upon the character of the irritant by which it has been induced, and into this question we need not now enter.

The arteries also undergo specific inflammations, and of these by far the most important are the syphilitic and the tuberculous. In the case of both of these infections it is commoner for the small arteries to be affected than for the large.

Syphilitic inflammation of the arteries affects so constantly the intima that the condition has come to be spoken of as endarteritis; and since one of the most characteristic changes which are induced by the syphilitic change is a stenosis of the vessel, the morbid process is called not only **syphilitic endarteritis,** but also **endarteritis obliterans.**

Endarteritis obliterans consists essentially in the formation of a focus of inflammatory tissue at some point in the wall of one of the smaller arteries. At first the inflammatory focus consists only of cells which have resulted from the proliferation of the endothelial cells constituting the deeper layers of the intima. Consistent with the syphilitic nature of the inflammation the process is a chronic one, and at the same time there is a marked absence of vascularity. As a result, caseation sets in and the focus of inflammation resolves itself into nothing more than a tiny gumma situated within the arteriole. Such a gumma is frequently excentric, but not invariably so; in any case it encroaches upon the lumen of the vessel. The change of itself never completely obliterates the lumen, and so far the name is misleading, but since the changes induced in the intima, together with the stenosis itself, are sufficient to lead to a thrombosis of the still patent portion of the lumen, the ultimate result of the change is that obliteration of the lumen which is indicated by the name.

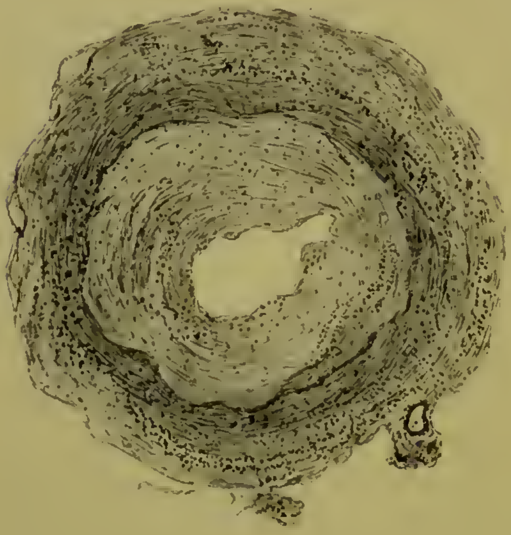


Fig. 72.—Section of Syphilitic Endarteritis (Endarteritis Obliterans). × 20.

The change principally affects the intima, which is enormously and irregularly thickened, and greatly reduces the calibre of the vessel. The media and adventitia are infiltrated with leucocytes.

Endarteritis obliterans is usually a somewhat widely spread process, but it does not, as a rule, give evidence of its existence except in the case of the cerebral arteries. When these vessels are affected, however, the results are equally striking and serious. How far this change is related to the degenerations it is impossible to say, but it is probable that there is a somewhat close affinity between endarteritis obliterans and the soft forms of atheroma.

Tuberculous arteritis also chiefly affects the small vessels, but it does not so commonly lead to a diminution of the lumen of the vessel as to the formation of a nodosity upon the surface. This is well seen in the case of tuberculous meningitis, in which the middle cerebral artery and its branches are frequently found to be the seat of a number of minute tubercles undergoing caseation in their centres. As a rule the tubercles are discrete, but in some cases they are present in numbers so large that the entire wall of the vessel becomes thickened and irregular. In these cases the lumen of the vessel is not obstructed, so that it is probable that the inflammation commences in connection with the vasa vasorum or the perivascular lymphatics of the arterioles. In yet other cases the tuberculous process is chiefly shown by a general infiltration of the vessel-wall by firm granulation tissue.

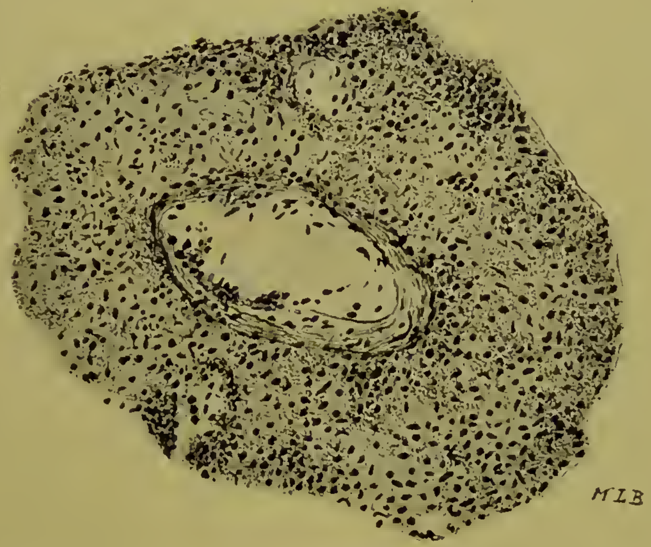


Fig. 73.—Section of Tuberculous Arteritis. × 420.

A minute vessel of the pia mater from a case of tuberculous meningitis. The vessel shows the presence in and around its wall of a relatively enormous amount of granulation tissue with fibroblasts and leucocytes. Caseation and giant cells are absent.

In this connection it is well to mention **peri-arteritis nodosa,** a condition which is not of very common occurrence, and which is chiefly seen to affect the arterioles of the lungs. The morbid change consists in the presence of a number of nodules of inflammatory formation on the outer walls of the arteries. In some instances, no doubt, the change is tuberculous, but in many it is probable that the tubercle bacillus plays no part in the process. Very little is known concerning the change beyond its anatomical characteristics.

(5) **New-growths.**—It is unnecessary to consider the neoplasms of the arteries here in detail. Reference has already been made

to those which are chiefly found to affect the vessels generally, and the arteries offer no particularities in this respect. Only one form of arterial new-formation need be mentioned—the cirsoid aneurysm. It consists in the formation of a tumour which on dissection is found to consist of a tortuous mass of newly formed arteries. The individual members of the mass show great irregularities in the diameters of their lumina, and, as might be supposed, pulsation is a constant and well-marked feature of the tumour. As a rule, the neoplasm is congenital, though, like the other vascular tumours, it is liable to increase rapidly in size after birth. Cirsoid aneurysms are extremely rare.

The remaining neoplastic affections of the arteries are in almost all cases secondary to some sarcomatous or carcinomatous focus that is developing in the neighbourhood, and, as such, call for no further consideration.

(2) THE VEINS

In connection with the veins it is necessary to consider only a small number of pathological processes, although it is important to note that the veins are accountable for a large proportion of the actual morbid processes that occur in the body.

(1) **Varix.**—One of the commonest changes which affect veins consists in an irregular dilatation of their walls, which causes them to become tortuous at the same time. The chief situations at which veins become varicose are the leg and the mucous membrane of the lower end of the rectum. In the former situation it is the saphena vein which is the seat of change, and in the latter it is the middle and inferior hæmorrhoidal. In these regions the veins sometimes become varicose without the intervention of any obvious factor, but it cannot be doubted that then, as in those cases in which the dilatation follows upon the presence of some obstruction to the venous return, the effective cause of the dilatation is the existence of an increased venous pressure. That this is so is easily seen by the fact that varicose veins in the legs are far more common in women than in men, and we shall probably be right in ascribing the liability of women to the facts of pregnancy and chronic constipation.

At the same time it is probable that there enters into the formation of varicosity some inherent peculiarity of the vein itself. What this peculiarity is we are unable to say, but we have reason to believe that the walls of the veins are in some persons less capable of resisting an increase in pressure than they are in others.

The chief alteration which takes place in varicose veins consists in a great thinning of their walls. This thinning is not equally distributed throughout the entire length of the vessel, but is quite irregular. At the same time there occurs at places a localised thickening of the wall which we must look upon as conservative. The result of these changes is that it is very difficult to obtain a number of sections of a varicose vein that are all cut in a direction perfectly transverse to the vessel itself, and even in the case of an approximately transverse section we are likely to find that there is an inequality of the wall so far as thickness is concerned.

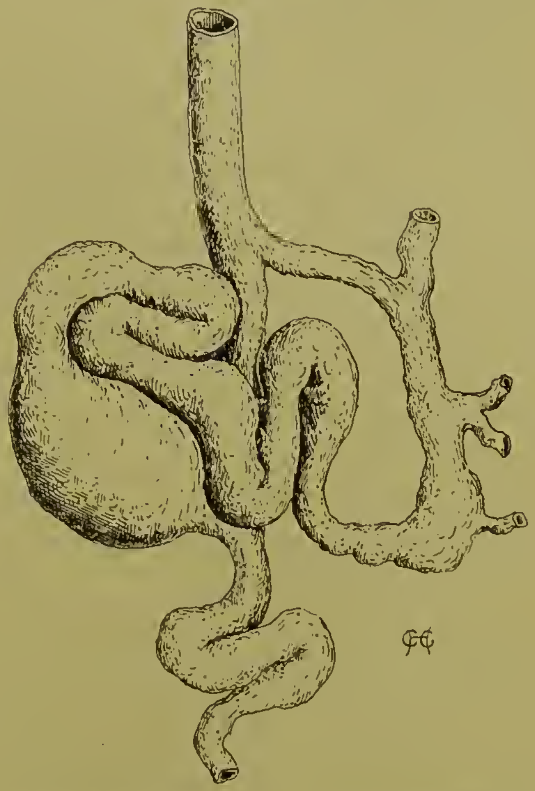


Fig. 74.—Portion of Varicose Saphena Vein. × $\frac{2}{3}$.

The vein is irregularly dilated and tortuous, and the wall is thickened.

Owing to the alteration in their walls, varicose veins are very liable to suffer in their nutrition, with the result that thrombosis is of common occurrence. This thrombosis may go further than the mere clotting of the blood, so that the clot may become organised and the lumen of the vessel completely obstructed by a mass of newly formed fibrous tissue. At the same time this fortunate termination may fail as the result of extension to the vein of an inflammatory process going on in the neighbourhood. In the latter case the clot is liable to undergo softening, and severe hæmorrhage may occur.

There are two especial factors which contribute to the readiness with which hæmorrhage occurs in the case of varicose veins, especially of the leg. The one is that the tissues which are normally drained by the affected vein are themselves lowered in nutrition owing to the changes undergone by the vessel, and are therefore less capable of withstanding the action of an irritant. The other is that the alteration in the vein leads to an atrophy of the valves, so that if the vein becomes opened an unobstructed exit is given to the blood in the iliac veins, and even in the inferior vena cava itself.

It has been said that the tissues which are drained by varicose veins are particularly liable to suffer in their nutrition. As a corollary to this statement it follows that they are often associated with ulceration. In the case of varicose veins of the leg this is especially true, and amongst the commonest of the minor ailments which are met with in the surgical out-patient practice of a hospital, varicose ulcers about the internal malleolus must be mentioned.

In the case of varicosity of the hæmorrhoidal veins—or shortly hæmorrhoids or piles—ulceration is not so commonly seen, whereas definite suppuration is far more usual than in the case of varicosity of the saphena. The reason of this difference lies in the greater vascularity of the mucous membrane of the rectum and in the particularly septic character of the materials with which it is normally in contact. A suppurating pile is almost always one which has become thrombosed and subsequently infected. At times the thrombus does not undergo suppuration, but becomes the seat of a deposition of calcium salts. It then becomes converted into a definite calculus and is termed a 'phlebolith.' Such concretions are met with most commonly in varicose hæmorrhoidal veins.

(2) **Phlebitis.**—Inflammation of the walls of veins almost always results from the extension of an inflammatory process in their neighbourhood. Its importance lies not so much in the actual inflammation as in the fact that it is necessarily accompanied by a venous thrombosis. Nor would this fact be of transcendent importance were it not that the conditions which induce it are particularly likely to be septic in a high degree. Hence the clot itself is very liable to undergo a septic softening, and under these circumstances we not only have the danger that portions may be detached from the main clot and, being carried into the main pulmonary vessels, may be the cause of sudden death, but also that smaller portions may be carried in the circulation to distant parts of the body, and, owing to the micro-organisms which they contain, set up a condition of pyæmia.

The walls of the veins in phlebitis become considerably altered. They invariably are thicker than normal owing to the accumulation between their coats of a large number of migrated leucocytes and much exuded fluid. When a vein has been the seat of inflammation, and has recovered, it is also thicker than normal, owing to the greater amount of fibrous tissue present in its walls.

Syphilitic inflammation is far less commonly seen in the case of veins than it is in the case of arteries, but in tuberculosis the veins often play a most important part. For it is often clear that the method whereby an originally localised tuberculosis becomes generalised is by way of the venous blood flow. This is particularly the case in those instances in which a generalised miliary tuberculosis follows upon the occurrence of tuberculous lymphatic glands in the neck or thorax. We frequently see that a caseous (tuberculous) bronchial lymphatic gland is so situated with regard to a vein that it is impossible for it, if it undergoes softening, to fail to empty itself into the adjacent vein (fig. 122). In addition, we not infrequently find definite tubercles upon or in the walls of such veins. It is only when a dissemination has taken place in some such manner as this that an opportunity is given for the formation of miliary tubercles upon the walls of the arterioles, such as occurs in tuberculous meningitis.

The veins are little liable to the various forms of degeneration. Atheroma is met with in them so seldom that it is almost a pathological curiosity. Even fatty patches which are not definitely atheromatous, and which are so frequently seen in the arteries, are very rare in the veins. With regard to the lardaceous and the other forms of degeneration, it may almost be said that they are unknown in the case of the veins.

(3) **New-growths.**—With the exception of the venous angeiomata the veins are not the seats of primary new-growths, whether non-malignant or malignant. Nor are they very frequently involved by new-growths starting elsewhere, if we except the pressure atrophy which they undergo in common with the other tissues. We do find in some cases, however, that a mass of new-growth finds its way into the lumen of the vein and, travelling in the direction of least resistance, grows along it for some distance. When such a condition obtains the growth is almost always malignant and rapidly growing, and it only occurs to any considerable extent in the case of the largest veins. A mass of pelvic sarcoma, for example, may penetrate into one of the iliac veins, and travelling in the direction of the blood stream, may occupy the greater portion or the whole of the inferior vena cava.

(3) THE CAPILLARIES

The morbid changes undergone by the capillaries are practically confined to those which form so conspicuous a portion of the phenomena of inflammation. To these we have already referred in detail elsewhere. There are, however, a few other conditions concerning these vessels to which a small notice may be given.

(1) **Congestion.**—The capillaries are of course affected in all cases of congestion, whether it be of the arteries or of the veins. Under these circumstances the principal histological characters of the tissue in which there is the congestion consist in the enormous number of widely dilated capillaries that come into view. This fact is especially well seen in the case of those tissues which are normally ill provided with blood. Such, for example, is the pleura. In the normal pleura, if sections are cut parallel to the free surface of the membrane, a far larger expanse of pleura is seen than if sections are cut, as is usually the case, at right angles to the free surface. Even with this large amount of pleura under observation the vascularity of the membrane appears to be inconsiderable. But if sections are made in a similar manner of a pleura which has covered a lung that has been the seat of hypostatic congestion, it is seen that the pleura is largely made up of a number of widely dilated capillary blood-vessels, which can be examined with ease. It is then seen that the congestion is accompanied by a great thinning of the already thin walls of the vessels. They do not, as a rule, show definite ruptures, although ruptures may obtain; nevertheless it is probable that a fair number of red corpuscles will be found outside the capillaries in addition to the enormous numbers that are still within them. (Fig. 13.)

(2) **New-growths.**—The only form of new-growth that affects the capillaries is the capillary nævus, and in this neoplasm, as will have appeared when we were considering the subject earlier, the newly formed vessels are very unlike the normal capillary in structure, owing to the much greater thickness of their wall.

Before leaving the capillaries, it may be mentioned that in the case of the blood condition known as hæmophilia it is uncertain how far the anatomical structure of the capillaries contributes to the constitution of the disease.

The essential feature of hæmophilia consists in the fact that hæmorrhage is liable to take place to an alarming, sometimes to a fatal, extent from a trivial lesion. Thus a patient with hæmophilia may bleed to death after extraction of a tooth. There is no doubt that in a large number of cases the essential factor in this disease is a deficiency in the coagulable power of the blood itself. But there are reasons for considering it as possible that the walls of the capillaries are themselves at fault in certain cases. Amongst these is the fact that some authors have described cases in which they discovered histological changes in the capillaries. The descriptions of the changes met with are, however, so indefinite and variable that it would not be profitable to describe them here.

(4) THE LYMPH CHANNELS

Strictly speaking, we ought to consider the morbid changes occurring in the extra-vascular lymphatic spaces apart from those which occur in the true lymphatic vessels including the thoracic duct. As a matter of fact, however, so little is known about the morbid histology of the lymph channels generally that it will be sufficient to consider them together.

Undoubtedly the commonest and most important change affecting the lymphatics is œdema. This condition bears a close parallel to the condition of congestion which obtains in the case of capillaries and veins. For in œdema the lymph spaces are over-distended with clear lymph and the tissue elements are widely separated from one another, while the lymphatics themselves are so full of lymph that they are easily recognisable with the naked eye. This is especially the case when the lymphatics concerned are those in the mesentery. For after food has been taken the lymph contains so large a proportion of fat that it becomes milky, and in cases in which there is some obstruction to the flow of lymph in the abdominal cavity, the over-distension of the mesenteric lymph channels becomes manifest by the presence of a number of fine white lines running in the peritoneal covering of the intestines and in the mesentery, up to the lumbar lymphatic glands or those in the hilum of the liver. Occasionally one of the lymphatic vessels becomes definitely cystic, so that a cyst containing creamy material and perhaps of the size of an orange is found in the mesentery.

Under certain circumstances the obstruction in the way of the flow of lymph is so considerable that the lymphatics become tortuous and widely dilated. This is particularly likely to be the case if an obstruction exists in the thoracic duct, and then the changes produced in the tissues are very marked. The chief condition under which such an obstruction of the thoracic duct occurs is when the parent worm of that hæmatozoon which leads to the disease known as **filariasis** is present in the cisterna lymphatica magna. There is then introduced a practically impassable obstruction in the way of the flow of the lymph from the lower part of the body. This lymph collecting in the lymph spaces of the tissues distends them considerably, and, being a nutritive fluid, leads to a great overgrowth of the connective tissue of the parts. This is particularly noticeable in the case of the skin, in which the overgrowth is so great that a condition is produced which is termed **elephantiasis**.

For the production of a local elephantiasis it is not essential that the obstruction to the lymphatic flow should be situated in the thoracic duct itself; it is clear that an obstruction of the main lymphatic channels of one of the lower limbs, for example, would be sufficient. When the obstruction is in the thoracic duct itself, we generally have the condition complicated by other factors. Thus it is probable that there will be in addition **chyluria,** or **chylous ascites,** conditions which depend upon the fact that the lymphatic vessels of the abdominal viscera have become dilated with chyle and have ruptured into the peritoneal cavity or the urinary bladder, as the case may be. It is clear also that the filarial obstruction may be so situated that chyluria, for example, results, apart from either chylous ascites or elephantiasis.

One of the most remarkable, as well as one of the rarest, conditions is that in which, owing to some obstruction, the lymphatic vessels of the entire mucous membrane of the alimentary tract become over-distended, tortuous, and prominent. The condition is known as **lymphangeiectasis,** and in it the mucous membrane has a shaggy appearance, the white and distended lymphatics standing out on the pink ground of the somewhat injected mucous membrane.

The walls of the lymphatics are occasionally the seat of definite inflammation (**lymphangeitis**). This only occurs when the part of which they are the absorbents is the seat of an intensely septic inoculation. The inflamed lymphatics then show up as red lines beneath the skin. The appearances are quite unmistakable, and are of grave importance. The chief seat at which they are seen is the flexor surface of the forearm.

Like the blood channels the lymphatic vessels are but little liable to be the seat of primary new-growths. Nevertheless conditions are known which correspond in many points to the venous and the capillary angeioma. These new formations are termed **hygromata** and **lymphangeiomata** respectively. Sufficient reference has been made to them elsewhere. In the extension of the carcinomata, however, they play a most important part. Thus in carcinoma of the breast, tiny nodules of growth are often found along the course of the lymphatics leading to the axillary glands.

SECTION IV

THE SPLEEN, THE LYMPHATIC GLANDS, AND THE THYMUS BODY

THE tissues which we are about to consider in the present section have much in common so far as their normal histological characters are concerned, but they differ greatly in respect of the morbid conditions to which they are severally liable.

(1) THE SPLEEN

From our scanty knowledge as to the functions of the spleen, we are constrained to believe that its main functions are hæmatopoietic, and are particularly bound up with the formation of leucocytes. In accordance with this view, we find that some of the most important alterations of the spleen are met with under conditions in which there are marked changes in the constitution of the blood. It is not the case, however, that a marked alteration of the blood is invariably associated with splenic changes. Nor is it at all certain how far, in those cases in which splenic changes are found, the alteration of the spleen is primary, how far it is secondary.

In the anæmia which follows upon severe hæmorrhage the spleen is always found to be small, shrunken, and pale. Its consistency is flabby and its capsule is shrivelled. Such an appearance is met with whatever may have been the cause of the hæmorrhage, so long as it has been produced with a fair degree of suddenness. One of the commonest conditions under which this variety of spleen is found is in cases in which the patient has been 'run over,' and has sustained a rupture of the liver, for example. Microscopically no alteration is to be found, except, perhaps, a diminution in the number of red blood corpuscles in the spleen pulp.

When the anæmia has been of a somewhat chronic type, the alteration of the spleen is in the direction of its enlargement. This is the case whether the blood change is in the leucocytes principally or in the red cells. Thus the two conditions under which the spleen reaches its largest size, viz. leucocythæmia (spleno-myelogenous leuchæmia) and ague, are widely different so far as the blood conditions which prevail in them are concerned. For in leucocythæmia there is an enormous increase in the number of leucocytes present, together with a moderate diminution in the number of erythrocytes, while in ague there is an enormous diminution in the number of red cells, owing to their destruction by the malarial parasite, and there is probably little or no alteration in the number of leucocytes at all.

But the remarkable point is that, although the malarial spleen may weigh five or six pounds, and the leucocythæmic spleen may be so large that it practically occupies the entire abdomen and weighs twenty pounds or more, the histological changes in the organ are very small. In the leucocythæmic spleen we shall probably find that there are larger numbers of granular leucocytes than is normally the case, and the malarial spleen will show a larger amount of pigment granules and degenerated red blood corpuscles than normal; but beyond these points there will be little or nothing to attract notice beneath the microscope. It is true that the larger amount of pigment in the malarial spleen will cause it to be of a darker colour than the leucocythæmic spleen, in which the excess of leucocytes causes the organ to be paler than normal, and that the Malpighian corpuscles are larger and paler in the leucocythæmic spleen; but this is all. The only really striking change is the great alteration in the size of the organ.

In some of the other forms of anæmia the spleen is also enlarged, though not to so great an extent. This is particularly the case in lymphadenoma (Hodgkin's disease), in which the organ may weigh a couple of pounds. The same is true in the little-known conditions summed together under the names of 'splenic anæmia' and 'splenomegaly.' In lymphadenoma it is frequently said that there is an increase in the amount of pigment present in the organ, whether in the fibrous-tissue stroma or in the Malpighian corpuscles, but this is a point which is frequently very difficult to make out.

A more important change in the spleen in lymphadenoma, when it occurs, is that which causes the formation of the so-called 'hardbake spleen,' from its resemblance to that sweetmeat. The change consists in the enlargement of the foci of lymphoid tissue in the organ, and the further addition of masses of lymphoid tissue of new-formation. As a result, the normal red or brown colour of the cut section of the spleen becomes modified by the presence of a number of foci of a white colour. These foci are of irregular size and shape, but most of them are about the size of the little finger nail. Readily distinguishable macroscopically, they are difficult to make out under the microscope, for they consist of nothing more than an agglomeration of lymphocytes, and, therefore, differ little from the general structure of the organ.

The appearance of a lymphadenomatous spleen, such as that which has just been described, is very similar to that of a spleen which is the seat of a number of caseous tuberculous foci.

Tuberculosis of the spleen manifests itself under three distinctly different forms. It may be that the tubercles are miliary, and then the spleen is affected along with the other organs in the course of a generalised miliary tuberculosis. Under these circumstances it is commonest for the tubercles to be most numerous immediately beneath the capsule of the organ. In the spleen pulp they are present in smaller numbers, but they are still present as may be determined by microscopic examination. Macroscopically, they are very difficult to make out owing to the resemblance between them and the Malpighian corpuscles. Owing to the frequency with which cases of generalised miliary tuberculosis are met with, particularly in children, this form of splenic tuberculosis is the most common.

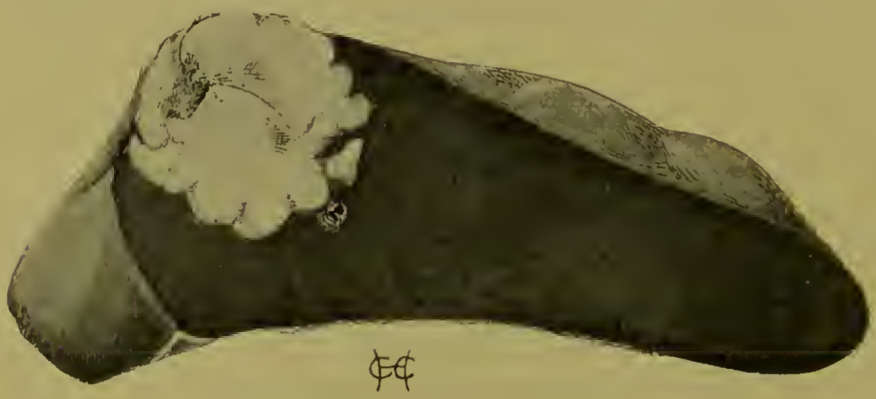


Fig. 75.—Caseous Tuberculous Mass in Spleen. Natural Size.
No other evidences of tuberculosis found in the organ.

Far less common, but still not rare, is that variety in which definite caseous foci are formed. This variety is chronic, and the caseous foci formed are similar to those which are met with in the lymphatic glands, in the substance of the cerebellum, and elsewhere. These caseous foci can only be distinguished from the lymphoid foci of the lymphadenomatous spleen by the aid of the microscope.

By far the most uncommon variety of tuberculosis of the spleen is that in which a number of foci of large but irregular size, and of a somewhat paler colour than the spleen pulp itself, are disseminated throughout the organ. It is certain that we have here the early form of the caseous variety. For it is found in some instances that a certain number of these red or brown foci have yellowish-white caseous centres. The interesting point is that the tuberculous mass present in this variety is as large as those present in the fully caseous variety. It appears as if the tubercle were not in this instance laid down in the form of miliary tubercles, and that the large foci were not formed as in the lung by the aggregation of a number of miliary tubercles, but as if the large focus of tuberculosis were laid down in mass. Microscopically such a mass of tubercle shows the complete absence of any trace of caseation. For the rest, it consists of a number of endothelioid cells and lymphoid cells, the former generally predominating, and, as a rule, a relatively large number of well-formed giant cells.

The remaining forms of inflammation do not often affect the spleen. Nevertheless abscesses are sometimes met with. Then, however, they result from the formation of a septic infarction. It follows that they are met with in cases of ulcerative endocarditis almost exclusively. Simple infarction is of common occurrence; it is rare to meet with a case of cardiac disease which reaches its normal termination, in which the spleen fails to show, at the autopsy, either the actual presence of recent infarcts or evidences of former infarction in the form of depressed cicatrices. As a rule infarctions of the spleen are large and of the anæmic variety; they frequently show central softening.

Besides the occurrence of infarctions, the spleen, in cases of chronic heart disease, manifests a certain hardness and firmness which is almost characteristic. On attempting to make a section the organ offers a notable amount of resistance to the knife and cuts with a grating sound. The spleen pulp is of a deeper red colour than normal, and the fibrous-tissue trabeculæ stand out more definitely than normal. Whether the organ contains an excess of fibrous tissue under these conditions is a matter of doubt, but there is no doubt that the increased hardness is largely due to the congested state of the organ; it is probable, on the whole, that the amount of fibrous tissue present is also increased.

The only other condition under which a similar change of the spleen is seen is that in which there is obstruction to the passage of the blood through the liver by the portal vessels. Under these circumstances, too, a chronic congestion of the spleen is produced. The condition which is of greatest importance in this connection is cirrhosis or chronic fibrosis of the liver. Whenever the spleen is thus congested the capsule of the organ becomes thickened and opaque. As a rule this modification of the capsule is equally distributed over the entire surface, but sometimes the thickening is irregular, and then the surface of the organ has a mottled and irregular appearance.

In the large majority of cases when the spleen is the seat of any morbid change it is enlarged. This fact has come out clearly in the conditions to which reference has already been made. But a number of diseased conditions are known in which the spleen, although enlarged and otherwise altered, is not affected to so obvious an extent. Thus in all the acute infective diseases there is a greater or less degree of enlargement of the spleen, accompanied, as a rule, by a softening of the spleen pulp. This is notably the case in typhoid or enteric fever, in which disease the enlargement is often sufficiently great for the organ to be palpable during life. In rickety children, too, an enlargement of the spleen is frequently present.

To the subject of lardaceous degeneration as affecting the spleen we have already sufficiently referred. Apart from lardaceous disease and the caseation which occurs when the spleen is the seat of tuberculosis, the organ is not liable to undergo degeneration.

New-growths of the spleen are very rarely met with, and primary new-growths are practically unknown. In the same way it is very uncommon for the spleen to be the seat of deposit of any of the entozoa, with the exception of the malarial parasite. In particular, hydatids are very rarely seen in the spleen. Occasionally, however, they are present, and then they may attain to considerable size.

It is very common for small bodies to be found in the immediate neighbourhood of the organ, which possess all the histological characters of splenic tissue, and only differ from the organ itself in point of size. These bodies are in reality accessory splenules, and they partake of the changes which affect the spleen itself. Thus we find them enlarged in typhoid fever, and hardened in chronic congestive conditions, while when the main organ is lardaceous, the splenules are similarly affected.

(2) THE LYMPHATIC GLANDS

Owing to their physiological position midway between the tissues, on the one hand, and the blood, on the other, it is readily intelligible that the lymphatic glands are frequently the seat of morbid change. For the same reason the vast majority of the diseases of the lymphatic glands are secondary and not primary.

Primary diseases of the lymphatic glands (with the exception of lympho-sarcoma) are practically confined to the one disease, lymphatic leuchæmia, and here it is quite a matter for discussion as to whether the blood changes which are present depend upon the modifications of the lymphatic glands, or whether the alterations of the blood and of the lymphatic glands are both secondary effects of some one primary cause which is not yet discovered.

On the other hand, it is certain that in the vast majority of cases in which inflammation is set up in the lymphatic glands, the change here is secondary to a local lesion in some distant part with which the particular lymphatic glands are in direct connection by means of the lymphatic vessels. Thus when an inflammation occurs in the lymphatic glands of the axilla we shall only in the very rarest instances fail to find a lesion on the corresponding hand of the individual. So much is this the case that we shall probably be right if we say that inflammation of the lymphatic glands (adenitis) is never primary.

Where the inflammation in the gland does not go on to suppuration, the alterations in the gland itself are almost entirely macroscopic. It is true that we may find some microscopical evidences of congestion, but these will probably be present rather in the connective tissue in which the gland lies than in the lymphoid tissue itself. Histologically, the differences between the normal and the inflamed gland are so slight that it is impossible to base a diagnosis of inflammation upon them alone. The same is true in lymphatic leuchæmia. But in both of these morbid conditions a considerable enlargement of the individual glands is seen, so that diagnosis of either condition from the normal is rarely a difficult matter. Diagnosis between the two conditions of enlargement themselves is also easy. For where there is adenitis, in addition to the enlargement some of the ordinary clinical signs of inflammation are present, and where there is lymphatic leuchæmia the modification of the blood, and the fact that the change is one affecting all the systems of lymphatic glands throughout the body, settle the question.

But, although it is relatively easy to distinguish between simple adenitis and lymphatic leuchæmia, it is sometimes very difficult to diagnose between each of these diseases separately, and certain other conditions. Thus when a mass of glands is present in one of the triangles of the neck, it is at times extremely difficult to decide whether we have to do with a tuberculous enlargement or one due to the existence of an infiltration by a malignant growth, in particular lympho-sarcoma. So, too, when we find a general enlargement of all the lymphatic glands of the body, it may be uncertain whether the case is one of lymphatic leuchæmia or one of lymphadenoma, or even one of lympho-sarcoma. In the latter instance the condition of the blood, so far as the numbers and the characters of the leucocytes are concerned, may,

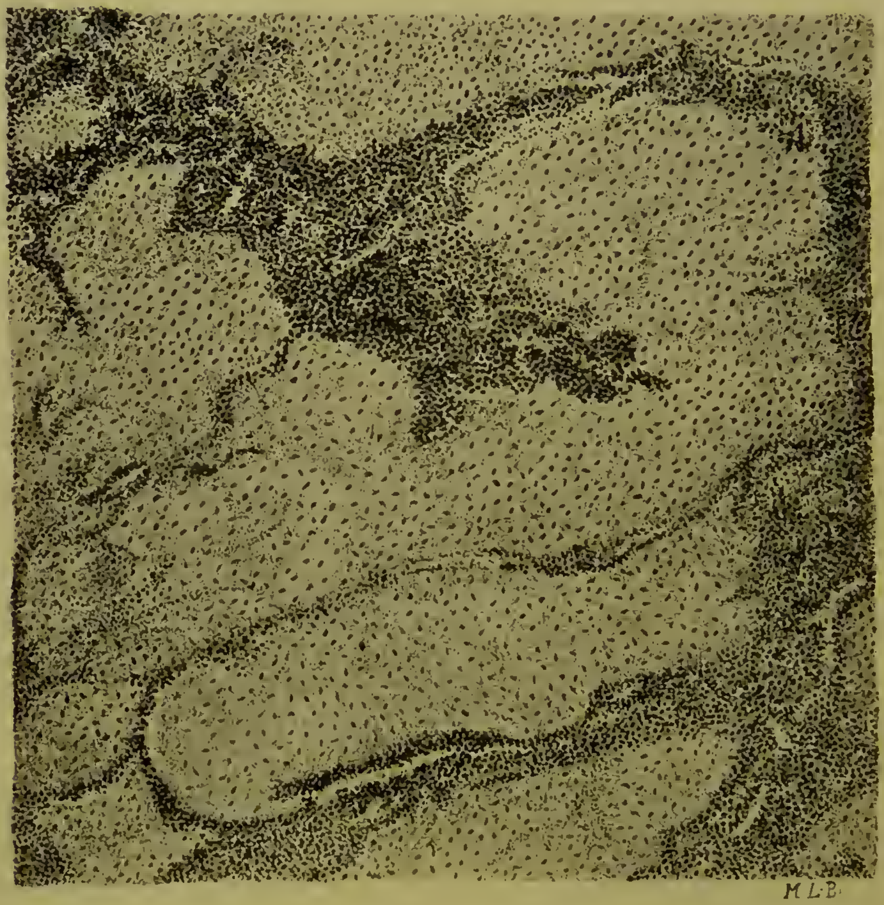


FIG. 76.—EARLY TUBERCULOSIS OF LYMPHATIC GLAND. × 120.

The greater part of the section consists of collections of pale-staining endothelioid cells, of which the elongated nuclei are easily recognisable; very few leucocytes and no giant cells are visible in this material. The dark highly cellular part is pre-existing lymphoid tissue of the gland. Ultimately the tuberculous granulation tissue would involve the entire gland and would undergo caseation.

or may not, give us assistance. Not infrequently, indeed, the actual diagnosis has to be left a matter of doubt to the end.

Amongst the especial varieties of inflammation the lymphatic glands are most commonly affected by tuberculosis and by syphilis. Tuberculosis of glands is an excessively common condition, particularly in young persons. We may find that the glands affected are cervical or bronchial or mesenteric. In the two former situations a chronic enlargement of the glands is probably due to tuberculosis, but in the case of very young children we often meet with enlarged mesenteric glands which are not tuberculous, but have become enlarged owing to the occurrence of a prolonged intestinal irritation. In the large majority of cases tuberculous glands are found to be so extensively affected that they are converted into masses of caseous material. Subsequently the caseous material may undergo softening (this is particularly the case with the cervical glands) or calcification. In any case it is quite uncommon to meet with glands in which the tuberculous process has not yet reached to the caseous stage. Rarely, however, one sees enlarged glands which are completely metamorphosed by the presence of numbers of large foci of tuberculous inflammation showing no trace of caseation.

The enlargement of the lymphatic glands occurring in syphilis is rarely so considerable as that which takes place in tuberculosis. At the same time the variety of change present is different. For the glands are hard from the presence in them of an increased amount of fibrous tissue of inflammatory origin. Caseation, softening, and calcification are very seldom met with in the case of syphilitic lymphatic glands.

Amongst the acute specific inflammations which are accompanied by enlargement of the lymphatic glands, the most important are diphtheria and typhoid fever. There is, in reality, nothing peculiar about these infections and the involvement of the glands, but it is so common for the glands at the angles of the jaws to be enlarged in cases of diphtheria, and for the mesenteric glands to be enlarged in cases of typhoid fever, that the glandular change has come to possess a certain amount of clinical significance from a diagnostic point of view. Suppuration of mesenteric glands in cases of typhoid fever are not very uncommon, but in diphtheria suppuration of the enlarged cervical glands is rare.

The new-growths involving the lymphatic glands are, in the main, secondary, and among the new-growths implication by carcinoma is far more common than implication by sarcoma. All varieties of carcinoma are liable to be found secondarily in the glands corresponding to the tissue in which the new-growth is primary. Thus we meet with carcinomatous axillary glands in cases of carcinoma of the breast, while the cervical glands are implicated in carcinoma of the tongue or lip, and the glands of the groin in carcinoma of the external generative organs. If a case lasts for a considerable time, systems of glands other than those directly affected become involved. Thus in a case of carcinoma of the lip, the thoracic lymphatic glands may become invaded by the disease after the cervical glands have become extensively involved.

When a gland which is little affected is examined microscopically, it is seen that the gland tissue presents the appearance of a number of separate foci of the new growth at different points in its substance. These foci are apparently independent of one another, and have arisen in consequence of the lodgment, at the seats of their formation, of a number of emboli derived from the primary growth. Subsequently the foci coalesce, and then the entire gland is converted into a mass of carcinoma that hardly differs in character from the growth which gave rise to it. The principal point of difference depends upon the fact that the growth of the cells and their multiplication in the gland are more rapid than they are in the primary growth. Glands which are secondarily affected with a new-growth do not show the same tendency to fusion as those which are primarily affected.

As we include endothelioma among the sarcomata, we may say that in this class of new-growth there is a liability for the lymphatic glands to be affected secondarily in sarcoma. With this exception, it is rare for secondary foci of sarcoma to be found in the lymphatic glands. As has been said, it is commoner for generalisation of the sarcomata to take place by way of the blood stream.

With regard to primary affection of the lymphatic glands by malignant growths, carcinoma is unknown. In the case of the sarcomata the only primary form of growth is lympho-sarcoma; it generally affects large tracts of glands or other lymphoid tissue. A very common situation for its occurrence is the mediastinum, and here the mass of new-growth may be so considerable that it ultimately kills the patient by mechanical interference with the action of the heart and lungs, as well as by the pressure which it exerts upon the important nerves present in the thoracic cavity.

Circumstances of great difficulty arise in those cases in which a system of glands that were at first enlarged as the result of a chronic inflammation becomes secondarily affected with lympho-sarcoma. This is not a very uncommon occurrence, especially in cervical glands which have become enlarged as the result of their infection by the tubercle bacillus. In a strictly inflammatory as distinguished from a strictly neoplastic affection of the glands the chief difference lies in the tendency of the glands to remain separate in the inflammatory affections, and to become fused in one mass in the neoplastic condition. But when the inflammation of a chain of cervical glands has gone so far that softening and abscess formation have occurred, the amount of inflammatory new material which is formed between the individual glands is sufficient to weld them into one general mass, and then there is the greatest difficulty in coming to a decision as to whether one has, or has not, to deal with a condition of lympho-sarcoma.

(3) THE THYMUS

In the case of this organ it may almost be said that we are totally unacquainted with its pathology. We know that, instead of undergoing atrophy during the first year of life, it may persist until perhaps the fifteenth or twentieth year. But even then we are unaware of the effects that that persistence has upon the individual in which it obtains.

In rare instances it not only persists, but also increases greatly in size. If the increase in size is unaccompanied by any other morbid conditions, it must be regarded as hyperplastic. In very rare instances such an enlargement of the thymus may be the effective cause of death. This is most likely to be the case in children in whom the neck is small and the thymus body proportionately very large, even under normal circumstances. When, then, in children the organ becomes greatly enlarged, it may cause compression of the heart or of the cardiac nerves, or perhaps may definitely interfere with respiration by pressing upon the trachea or bronchi.

In still rarer instances the morbid enlargement of the thymus is associated with other conditions, the most important of which are an anæmia of severity and a localised formation of foci of lymphoid-like tissue in various parts of the body. As to the actual significance of such cases it is difficult to speak with certainty. It is possible that we have to do with a sarcomatous condition starting primarily in a persistent thymus, and then the localised deposits in the other organs must be regarded as secondary and also malignant; under these circumstances we should have a condition very closely allied to lympho-sarcoma, and the accompanying anæmia would be, so to speak, accidental. But it is also possible that the anæmia is not accidental in the same sense, and that the enlargement of the thymus and the other lymphoid tissue is akin to that which occurs in lymphadenoma or in lymphatic leuchæmia. Under these circumstances we should have to regard the thymic condition rather as neoplastic than as hyperplastic.

SECTION V

THE PATHOLOGICAL ANATOMY AND HISTOLOGY OF THE BONES

(1) **Degenerative changes.**—Leaving on one side for the present those changes which consist in a faulty development of the bone, it may be stated that the chief of the strictly degenerative changes to which bone is liable is atrophy, the result of pressure or of disuse. One form of atrophy from disuse which is of so constant occurrence that it may be denominated physiological is that which accompanies the onset of old age. In old age there is not only an actual diminution in length of the long bones, but also a marked diminution in their density. This can be well seen in the case of the femur. For, on making a longitudinal section of the head of the bone, and comparing it with a similar section of an adult femur, it is clear that the cancellous tissue shows wider spaces between its meshwork, and that the thickness of the hard bone of the shaft is less. Senile atrophy of the bones is a well-marked condition, but it must not be considered that an atrophy is the sole change which the bones may undergo in old age; we shall have to point out later that in certain cases the bones may become far thicker and denser than normal. Even in an uncomplicated case, it is usual for these two opposite processes to occur at the same time in the same individual. Thus we may find the long bones markedly atrophied and the bones of the skull thick and dense.

Atrophy from pressure we have already spoken of when considering the pathology of aneurysm. But the changes that were there mentioned were only special examples of the general law that a tissue which is exposed to a constant but intermittent pressure becomes absorbed. The process is so slow in the majority of cases that we are unable to detect it in actual progress, although the final result is obvious enough. Nevertheless there is every reason to believe that the process is carried out by the intervention of those cells (osteoclasts) which are normally occupied with the removal of bone. The process is fundamentally the result of two opposing forces, the one destructive, the other nutritive and constructive. The latter force is interfered with owing to the obstruction which the aneurysm or other mass presents to the nutrient blood-vessels of the bone, and as a result the destructive force obtains the predominance.

It is impossible to enter into any consideration of the relative frequency with which the individual bones are liable to atrophy. For any bone may be so affected. Nevertheless it is clear that those bones which are most closely placed in relation with blood-vessels liable to become the seat of aneurysm and in connection with those tissues and organs which are most liable to become affected by the various kinds of solid growth, are particularly those which will most frequently be the seat of a pressure atrophy. At the same time it is clear that, even though any bone may be affected by atrophy, those will be affected to the greatest extent whose density is least. Agreeably with this, we shall find that absorption takes place more readily of the bodies of the vertebræ than of the layers of dense bone which lie next the inter-vertebral discs, and that the ends of the long bones are more frequently and more extensively affected than the shafts. So, too, because the encephalon is but rarely the seat of a solid growth, we shall expect that the skull bones will be largely exempt from pressure atrophy, but we shall equally expect that it will occur whenever the ventricles of the brain become widely distended, owing to the accumulation in them of large quantities of cerebro-spinal fluid (e.g. chronic hydrocephalus).

These modifications of bones have, however, nothing which differentiates them, in reality, from the processes which go on in any other solid tissue under similar circumstances. There are nevertheless cases in which the bones become affected with a variety of degenerative atrophy which has no exact parallel in the other tissues. These changes constitute the rare condition known as **osteomalacia.**

Osteomalacia.—Osteomalacia is one of the most formidable as well as one of the most intractable of the pathological conditions to which the bones are liable. Fortunately it is also one of the rarest. The change consists in a softening of the bone owing to a removal of the inorganic—and in some degree of the organic—constituents. This softening may proceed to extreme lengths, so that the bone no longer is endowed with its characteristic rigidity, but becomes converted into a substance of the density of fairly thick fibrous tissue. At the same time there is also a diminution in the thickness of the bone, so that ultimately the shaft of the femur, for example, may be no thicker than paper. In the example figured in the text the loss of rigidity was so great that on slightly shaking the glass jar in which the specimen was contained, the lower part of the femur swayed from side to side independently to a large extent of the upper part.

The change in osteomalacia affects the central portion of the bone more than the peripheral. Hence there occurs a marked widening of the medullary canal of the long bones. In a marked case large quantities of the inorganic constituents of bone make their appearance in the urine.

Of the long bones, the femora, tibiæ, and fibulæ are the most liable to be affected, but in addition to them there is a great tendency for the disease to be present in the bones of the pelvis. In the case of the pelvic bones the diminished rigidity of the bones is, at the first glance, less obvious. But, on the other hand, there is always to be seen a more or less marked alteration in shape of the brim of the true pelvis occasioned by this loss

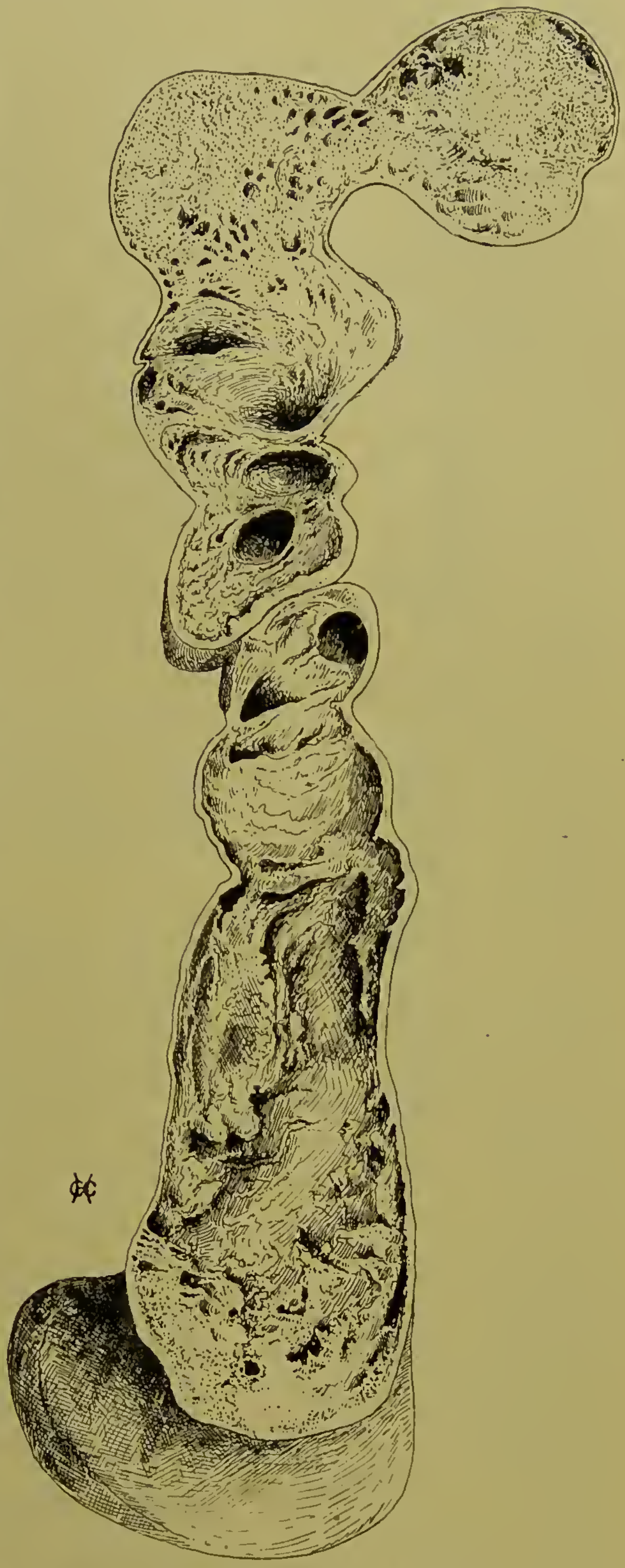


Fig. 77.— Osteomalacia of Femur. × $\frac{2}{3}$.
Except towards the two extremities, hardly any true bone is present. The bone of the shaft has been replaced by fibrous tissue.

of rigidity. For the softened bones yield before the pressure exerted by the femora and their attached muscles, and are pressed inwards until it frequently happens that the internal surfaces of the acetabula are almost in apposition. In this way a characteristic deformity of the pelvis is produced.

In the case of the short bones the actual histology of the change is better seen than it is in the case of the long bones. In the short bones, although the general outline of the bone is to a certain extent preserved, the bone substance itself becomes so spongy that it can be easily cut with a knife. At the same time it is so greatly diminished in specific gravity that it may float in water. The reasons for these alterations are seen on making microscopic examination of a portion of the bone, for it then becomes clear that the change consists in a widening of the Haversian canal, together with a decalcification of that portion of the bony structure which lies next to the canal itself, and a deposition of fat in the spaces thus formed. In some cases the bone marrow is replaced by a material which is red in colour, and seems to be of an inflammatory nature.

The disease is one of adult life, and seems to have some special connection with pregnancy. A similar, or perhaps the same, condition is met with in connection with insanity, and it is by reason of the softening which occurs that fractures of bones are frequently seen in asylums.

A curious point in connection with the fractures that occur in this condition is that when repair takes place the newly formed bone is of a normal type, and does not conform to the type of the altered bone in which the fracture has taken place.

(2) **Inflammation of bone (osteitis).**—It has already been said that there is no peculiarity in the inflammatory changes which affect bone other than those which depend upon the rigidity of the tissue in which the inflammation is going on. Nevertheless, when we come to consider the different specific forms of inflammation, we find that there are certain differences which serve to differentiate them from one another.

Since there enter into the formation of a long bone, for example, the periosteum, the bone proper, and the endosteum, with the medulla, it follows that we may have a periostitis, an osteitis, and an osteomyelitis. Sometimes we meet with the conditions more or less separate from one another. Thus it is common for syphilitic manifestations to affect the periosteum, for tuberculosis to affect the bone proper, while one of the most formidable diseases of childhood consists in a septic osteomyelitis.

It is true that the other portions of the bone suffer later in the large majority of cases, but there is no doubt that at first the disease may be strictly localised.

In the case of all varieties of inflammation of bone we find that destructive and formative processes are at work side by side, though the extent to which the one or the other of these processes predominates depends upon a number of circumstances. Where the destructive processes are in the ascendant there occurs either caries or the formation of a definite sequestrum; where the formative processes predominate (i.e. where the formative processes are particularly directed upon the periosteum) there is a new formation of bone.

Hence it follows that in every case of osteitis we must look for signs of caries at the point at which the irritant acts with the greatest intensity, and hyperostosis at the point at which the irritant action merges into that of a stimulus.

In those forms of inflammation of bone which may be spoken of as *simple*, meaning thereby those which are either aseptic or are associated with the ordinary pyogenetic micrococci, we generally find that new formation of bone is a marked phenomenon, however well marked caries may also be at the same time. An exception must be made in the case of septic osteomyelitis, which is usually associated with the **Staphylococcus pyogenes aureus**; for in this disease there occurs not only a suppurative alteration of the entire medulla and, probably, an acute necrosis of the whole diaphysis of the bone, but also so small a degree of new formation of the bone that it is represented by a congestion of the epiphyses and the periosteum. Nevertheless, even in this

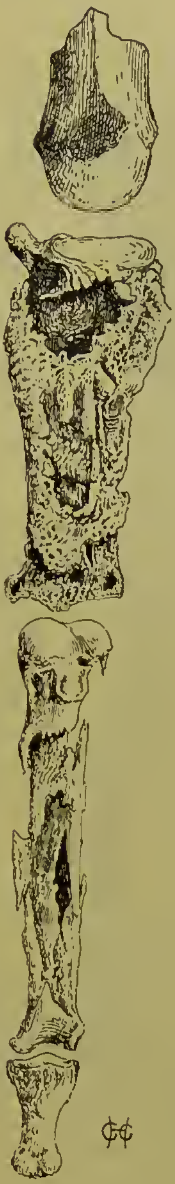


FIG. 78.—CARIES OF PHALANGES. NATURAL SIZE.

The result of a whitlow. In the second phalanx there is hardly any evidence of formative processes, but in the proximal a considerable new formation of bone has taken place as the sequel of the periostitis.

case the law holds good; for if the necrosed shaft of the bone, apart from the periosteum, be removed surgically, and the patient survives, the entire shaft of the bone is re-formed by the periosteum.

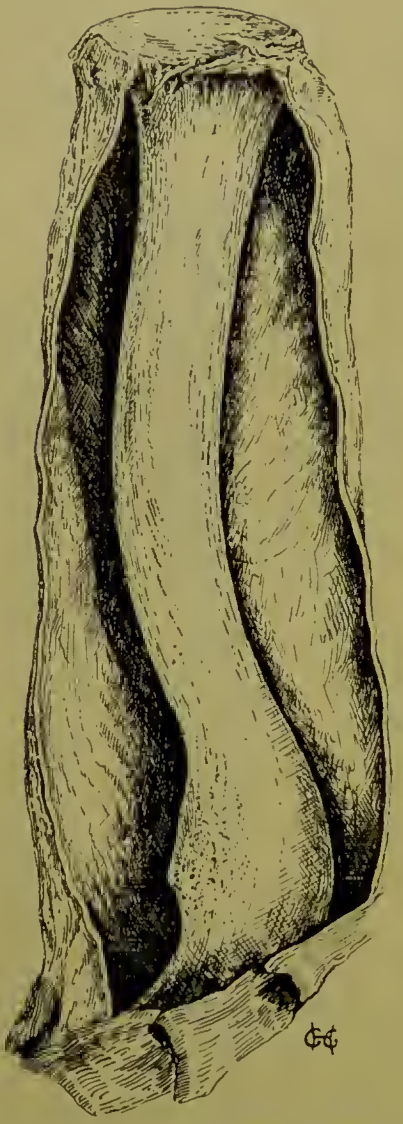


FIG. 79.—SEPTIC OSTEOMYELITIS. × $\frac{3}{4}$.

As the result of the septic processes the clavicle has necrosed and lies in an abscess cavity formed by the periosteum, which is itself much thickened and distended.

In the cases of syphilis and tuberculosis of bone the matter is somewhat different. For whereas in the simple inflammations we usually meet with the two processes in juxtaposition, in syphilis we more commonly find that either the destructive or the formative so largely predominates as practically to constitute the entire change, and in tuberculosis we find that the formative process is hardly ever manifested in more than a most rudimentary form.

Syphilis may affect any bone in the body, but it is most commonly seen in connection with the long bones (particularly those of the lower limbs) and the bones of the skull. In all these situations the actual disease of the bone generally commences as a gummatous affection of the periosteum, and extends to the bone itself subsequently. Such gummatous formations are termed **nodes** and are most commonly to be found upon the subcutaneous surfaces of the implicated bones. Besides the long bones of the lower limbs and the bones of the skull, the clavicle is a favourite seat for the formation of a node. It is probable that local injury plays a considerable part in determining the seat at which a node shall be formed.

At first a node is a collection of granulation tissue situated in the deeper layers of the periosteum, which readily undergoes caseation in some cases, while in others the inflammatory congestion of the periosteum is followed by so definite a formation of new bone that the node becomes converted into a boss of dense bone. In other cases, along with the caseation of the node there occurs a localised necrosis of the underlying bone, with the formation of a focus of caries or a definite sequestrum.

Although we may meet with syphilitic caries of any bone, it is usually most notable when it affects the bones of the skull. In this situation the change may be late secondary or definitely tertiary. Late secondary manifestations are responsible for those destructions of the bones of the palate which constitute so severe a portion of the results of untreated syphilis, while the tertiary stage of the disease is characterised rather by caries of the bones of the vault of the skull. Where the bones are thin, as in the palate, the caries affects the entire thickness, and consequently there is a total disappearance of portions of the bones affected, but where the bone has a definite thickness, either the whole thickness or only a portion of its surface may be removed. Therefore, in the case of the skull we have two forms of syphilitic caries, the one purely superficial and leading to a worm-eaten appearance, which may be present over a very considerable area of the outer surface of the vault, the other a destruction which leads to the formation of definite lacunæ with irregular edges and often as large as a five-shilling piece. These lacunæ are apt to be numerous, and the resulting appearance of the macerated bone is quite characteristic of the affection. The same is true of the worm-eaten appearance to which reference has been made. (Fig. 23.)

In the case of the long bones it is true that a caries also occurs, but usually it is largely masked by the existence of a new formation of bone of intense hardness. The resulting condition is frequently termed **sclerosis**. It consists essentially in an increase in the thickness of the bone surrounding the pre-existing Haversian canals, together with a new formation of bone of a similar denseness, as the result of the chronic congestion to which the periosteum has been subjected. At the same time the result is partly due to the fact that the periosteum has itself become altered by the existence in it of a syphilitic inflammation. Owing to the causes which underlie its formation, this sclerosed bone has not the smooth and regular surface of normal bone. Hence a tibia, for example, which is the seat of a syphilitic osteitis, weighs, perhaps, twice as much as a normal tibia, is much harder to saw through, shows an irregularly nodulated external surface of great density, and an internal surface which is highly irregular, and which may be composed of bone which is denser or less dense than normal.

In the subjects of congenital syphilis affections of bones also occur, but the changes are somewhat different in distribution, though not in pathology, from those which occur in acquired syphilis.

By far the chief seat for the occurrence of bone changes in congenital syphilis is the root of the nose, and since the disease in this situation is accompanied by pronounced caries, the ultimate result is a disappearance of the bridge of the nose. It is the presence of this disease of bone which is the cause of the 'snuffles' which are so characteristic an affection in syphilitic infants.

Another manifestation of congenital syphilis is seen in an alteration of the density of the bones of the vault of the skull. This change is produced with considerable slowness, and consists in a combination of the processes of atrophy and hypertrophy. In certain portions the bone may be so thin that it can easily be depressed by the finger, and in a macerated specimen is quite translucent and of the thickness of paper only, while in other portions there is a new formation of bone which causes the local formation of bosses. The thinning process is generally most manifest over the occipital bone, while the bossing is generally most marked over the parietal eminences. Nevertheless the changes need not show so regular an arrangement. The condition is known as 'Parrot's bossing,' or 'craniotabes.'

In addition to the modifications which have been described as characteristic of craniotabes, the subjects of congenital syphilis are also apt to present a general alteration of the contour of the entire skull. The principal feature of this is a prominence of the frontal eminences and a broadening of the entire forehead. The cause of this alteration is, in part, the existence of such changes as have been described, but it is also, in part, due to the fact that the general processes of nutrition in syphilitic children are ill carried out. As a result, the ordinary processes of ossification of the bones of the skull are apt to be abnormal, and the alteration may take place in the direction either of insufficiency or of excess. In a large number of cases the two conjoin, so that not only is there a deficiency of bone formation to close the fontanelles, but also there is a premature synostosis of the bones at the base of the skull, particularly the basi-occipital and the basi-sphenoid. Under these conditions the growth of the brain leads to an expansion of the fontanelles and a tilting forwards of the two portions of the frontal bone. Although these latter changes are frequently seen in cases of congenital syphilis, they are not exclusive products of the disease.

Tuberculous disease of bones differs principally from syphilitic disease in the fact that sclerosis is almost characterised by its absence. To a certain extent, as will be seen, a new formation of bone takes place even in tuberculosis, but the principal change is a comparatively slow and progressive caries. Sequestra are not often formed, and even when they are formed, they are usually of very small size. Tuberculous necrosis of bone is, unlike syphilitic necrosis, almost always accompanied by a destruction of the soft tissues overlying the affected bone and the formation of a more or less definite bone abscess.

A further difference is found in the fact that, whereas the syphilitic process commonly begins in the periosteum, in tuberculosis the periosteum is hardly ever the seat of commencement of the disease. Upon this point we are not able to speak with absolute certainty, but there is great reason to believe that the tuberculosis in a large number of instances commences in the actual substance of the bone. Thus in tuberculous disease of the vertebræ it is certain that, although the disease may occasionally commence in the inter-vertebral disc, or in the plates of denser bone which form the upper and lower surfaces of the body, it generally commences in the actual body of the vertebra.

There is a greater diversity among the bones that are liable to be affected with tuberculosis than among those liable to syphilitic manifestations. The femur, tibia, and fibula, the bones of the tarsus, the vertebræ, and the skull are particularly liable to tuberculous caries; the phalanges of the hand are also liable to be affected, but less commonly. In addition to the primary affections of the bones, they are almost always secondarily affected to a considerable extent, and always to some extent when the articulations are the seat of tuberculosis.

It is never found that a focus of tuberculous disease of bone shows a considerable formation of new bone in the neighbourhood of the principal seat of the disease. The utmost that we see is the presence of a few osteophytic growths. It must not be inferred from this that there is a complete absence of repair in connection with tuberculosis of bone, for this is not the case. In those instances in which the tuberculosis becomes stationary or recedes, a repair of bone occurs similar to that which occurs in the repair of a simple fracture. Thus in the case of tuberculous disease of the bodies of the dorsal vertebræ there occurs a caries of bone which frequently involves three or even more bodies. Those in the centre of the focus of disease disappear by a process of molecular disintegration, and the less injured portions above and below are brought into contact by the pressure of superincumbent parts and the action of muscles. If, then, the parts are kept at rest so that the irritant action is reduced to a minimum, the reparative powers of the tissues, combined in particular with the stimulative hyperæmia of the periosteum of the opposed portions of bone, are sufficient to lead to a synostosis and a definite repair of the injury. Owing to the fact that it is the bodies of the vertebræ that are especially affected, while the spines and the lateral processes escape, the form of the vertebral column as a whole undergoes a marked alteration which is characteristic of the condition. It presents a more or less sharp angle backwards, the apex of which corresponds to the spine of the vertebra of which the body was the most extensively diseased. The condition is now known as **angular** or **Pott's curvature** of the spine.

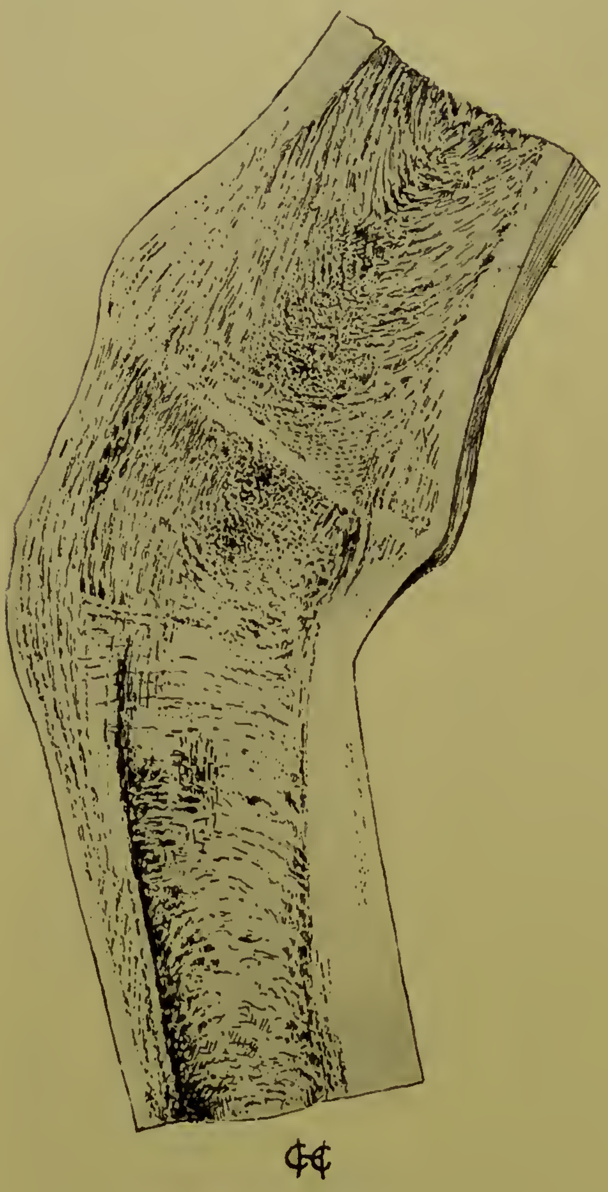


Fig. 80.—Synostosis. × $\frac{2}{3}$.

Bony union between femur and tibia after excision of knee. The curvature is the effect of bearing the weight of the body during the growing period of the bone.

Practically any portion of the vertebral column may be the seat of tuberculous disease, but the commonest situations are the middle and lower dorsal regions. The lumbar and cervical vertebræ are less commonly affected, but still disease in them is not rare. In the case of the cervical vertebræ the disease is especially apt to affect the atlas, axis, and the corresponding portions of the base of the skull. In such a case we may find that the caries is very extensive, so that little of the sphenoid bone, which is relatively less dense, remains. Nevertheless, as might be expected from a consideration of the important parts that are liable to be indirectly affected by disease in this situation, death not uncommonly occurs before there has been time for the production of any large amount of caries.

When tuberculous disease of bone occurs, it is of course necessary that the products of disintegration should be removed. Collecting at the seat of their formation, they produce, along with the inflammatory materials which accumulate in the progress of the disease, a liquid accumulation which has already been described as a 'cold' abscess. The actual situation of such an abscess, and the direction in which it will point, will, of course, depend largely upon the seat of the disease. But in the case of the vertebral column there are certain well-recognised situations in which the abscesses connected with disease of special regions of the column are commonly found. Thus when the disease affects the lower dorsal vertebræ, it is usual for the pus to track along the course of the anterior roots of the nerves corresponding to the affected vertebræ, and since these in the region under consideration pass into the substance of the psoas muscle to form the lumbar plexus, the resulting abscess occupies the substance of the psoas muscle. Since, too, it is easiest for it to extend along the fibres of the muscle, it ultimately passes beneath Poupart's ligament and comes to point superficially in the groin.

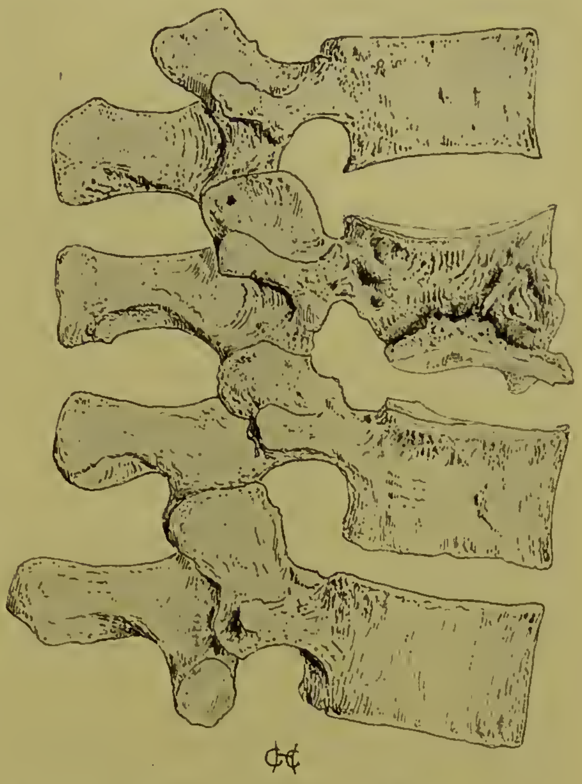


FIG. 81.—EARLY CARIES OF VERTEBRA. × $\frac{3}{4}$.

The existence of the primary focus in the body of the vertebra is well shown. A certain amount of new bone has been formed on the front of the body of the bone alongside of the caries. The condition was tuberculous.

In a similar way purely anatomical considerations determine the facts that when there is disease of the lumbar vertebræ, the abscess points in the loin after having passed along the spaces between the planes of lumbar muscles, and that when the upper cervical vertebræ are affected the abscess points in the pharynx.

Histologically, the appearances of tuberculous disease of bone partake of the characters of tuberculosis generally and of those of ordinary inflammation of bone. That is to say, we find that the caries which occurs is carried out by the action of osteoclasts, but the osteoclasts are of a kind that cannot be distinguished from the giant cells of tuberculosis. At the same time, that caseation which is characteristic of tuberculosis, and so relatively uncommon in the ordinary inflammation, may be a marked feature. Generally, however, the most that we can find is a caries into the production of which the formation of granulation tissue enters largely. We may be able to find upon careful examination a few tubercles with classical composition; we may, though it is very improbable, be able to find the tubercle bacillus, but in all probability we shall be able, from histological examination alone, to affirm nothing more than that the condition has been produced in the course of a chronic inflammation. The actual nature of the disease will far better be determined by attention to the macroscopic characters of the lesion.

Of the other infective inflammations **actinomycosis** is the only one which calls for remark here. Along with actinomycosis we may also consider the disease known as **Madura foot** (fig. 26). Although it is probable that the micro-organism which causes Madura foot is not the actinomyces, the difference between them is so slight that by some authors they have been considered as identical. In any case the histological characters of the lesions produced by them are practically the same.

Madura foot, as its name implies, is a disease which especially attacks the feet, but it is also found on the hands. It is a disease of tropical climates, and is principally met with in the case of the coloured races who go barefoot. The disease commences as a small swelling which, after a shorter or longer time, bursts, and gives exit to a sanious discharge in which small round black bodies are to be distinguished. Ultimately the disease may spread until it has involved the entire leg, converting it into a thick brawny mass, with irregular skin surface, and numerous sinuses reaching down to the bone. At first, however, the disease is superficial.

In actinomycosis, allowing for the difference in the situations of the disease, the appearances are closely similar. There is a thickened brawny condition of the part and the overlying skin, and numerous sinuses lead down from the surface to the deeper parts, and in a large number of cases down to diseased bone. The sinuses also give exit to a thin pus, which may be slightly mixed with blood, and in this pus white, round, and fairly hard grains may be found, which, on examination, show themselves to be the actinomyces fungus. When it is added that in certain cases of Madura foot the grains are not black but white, it is clear that the closest resemblance obtains between the two conditions.

In the case of bone affected by either disease, the condition produced is one of slow caries. Reparative and hypertrophic characters are almost completely absent; in this respect the diseases having a good deal in common with tuberculosis. The actual destruction of bone is brought about by the formation of a granulation tissue, the characters of which differ somewhat in different cases. In one case we may find that little else is present beyond a collection of small round cells (leucocytes), and the focus of disease looks exactly like an early abscess of the ordinary kind. In other cases we may find that there is a definite formation of young connective tissue, while in yet others, giant cells may be present in considerable numbers, and well formed. As a rule caseation is not a marked feature; the progress of the disease is sufficiently fast for the formation of pus to be the characteristic termination.

Rickets.—Rickets is a disease which is practically always met with in children under three years of age and above nine months. Nevertheless its results persist into adult life, and produce certain important modifications of the shapes of the bones. As to whether rickets occurs earlier than about nine months there is a difference of opinion. Some authors hold that the condition may be contracted *in utero*, so that they recognise a condition of 'fœtal rickets.' Other authors maintain that the condition seen in the fœtus is not true rickets, but differs in certain essential points therefrom.

Rickets consists essentially in an alteration of the processes going on in the line of ossification of the long bones and in the centres of ossification of certain of the short bones. In most cases it is characterised by the formation of a young osseous material which is excessive in quantity but deficient in quality. In some cases, however, where the disease is very marked, not only is a deficiency in quality met with, but also a deficiency in quantity.

More or less all the bones of the body are liable to the rickety change, for the underlying condition upon which it depends is one of nutrition generally. Nevertheless certain bones are so much more liable to become affected than others that they alone attract notice.

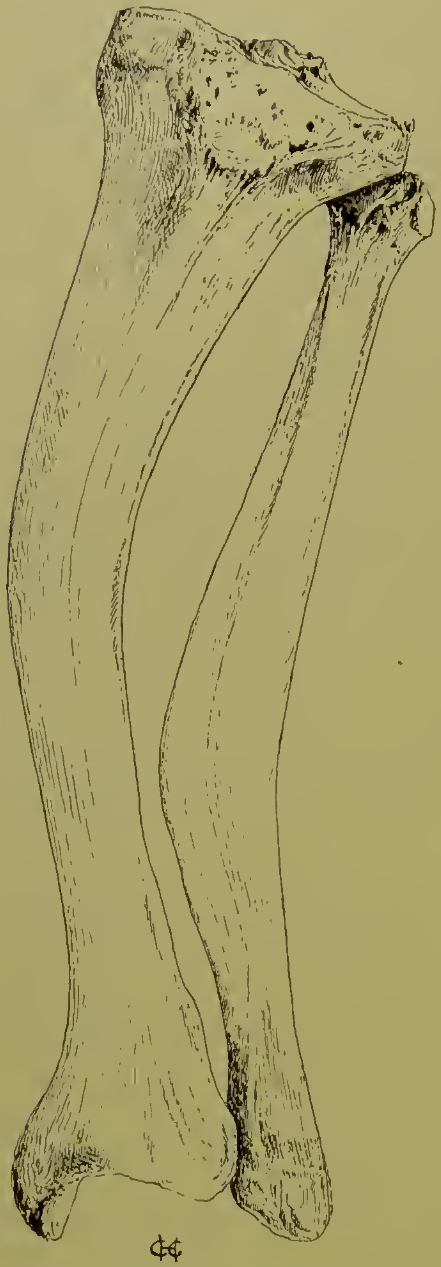


Fig. 82.—Bone in Rickets. × $\frac{2}{3}$.

The tibia and fibula are flattened and curved inwards. The fibula lies almost alongside of the tibia instead of almost behind it. The bones themselves are firm and strong. From an adult who suffered from rickets in childhood.

The chief bones to be affected by rickets are the radius, the tibia, the ribs, the bones of the pelvis, and certain bones of the skull, particularly the frontal and parietal bones. Less commonly the disease affects the femur and the humerus, while the remaining bones of the body are only affected on rare occasions.

The actual process can best be understood by examining one of the long bones, and for this purpose a rib is the most convenient. Such examination shows that the seat of the disease is at the junction of the bone with its cartilage. At this spot there is a definite swelling which is commonly more marked upon the internal surface of the bone, but yet is sufficiently well marked in most cases to be distinguishable during life by running the finger down the front of the thorax at the junction of the costal cartilages with the ribs ('rickety rosary').

On making a section through the bone and its cartilage it is seen that the excessive amount of tissue consists of cartilage and not of bone. At the same time it is recognised that the line of demarcation between the bone and the cartilage is not well defined and narrow, as is usually the case, but, on the contrary, is irregular and broad. Lastly, it is often seen that the bone itself is redder than normal, both as concerns the medulla and the periosteum, and that the line of demarcation between bone and cartilage is not pale as is normal, even in young children, but is definitely congested.

Microscopic sections of the affected area demonstrate that the change consists in an irregularity of the processes occurring in the line of ossification. It is no longer sharply defined from the fully formed bone on the one hand, and from the cartilage on the other. It extends irregularly into portions of cartilage which have not for the most part become involved in the ossification, and towards the bone detached islets of cartilage of various size and of irregular shape are present in the midst of a definite bony formation.

At the same time there is not the orderly arrangement of the cartilage cells in lines at right angles to the line of ossification which is characteristic of the normal process. On the contrary, the cells do not appear as if they were dividing in one direction, but in all; nevertheless the general tendency for division of the cartilage cells in a direction at right angles to the line of ossification still persists.

Partly independently, and partly as the result of the alteration in the mode of division of the cartilage cells, the blood-vessels which penetrate between the columns of cartilage cells do not, on their part, maintain their normal orderly arrangement. They are more irregular in size, and far more irregular in the directions which they take. As a rule, their diameter is greater than

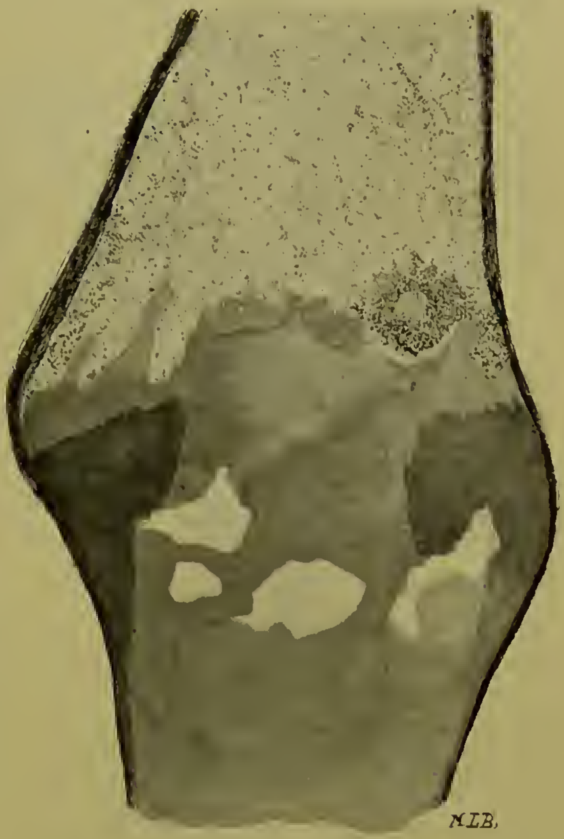


Fig. 83.—Section of Rib in Rickets. × 6.

The portion between the bone (above) and the clear spaces (below) constitutes the widened and very irregular zone of calcification. The bone is less dense than usual and the periosteum is somewhat thickened. Irregular agglomerations of leucocytes with an islet of bone in one of them are found close to the line of ossification. The hyaline cartilage is very uneven in its staining, partly owing to great differences locally in the number of cartilage cells, partly owing to varying degrees of calcification. The white spaces in the cartilage are excessively large and irregular medullary spaces. Below the medullary spaces the hyaline cartilage is fairly normal.

normal, and this accounts for the hyperæmia which is present about the line of ossification.

Nor does the actual formation of the bone proceed in a normal manner. The osteoblasts are more irregular in size and shape, and are fewer in number than normal, while the osteoclasts are more numerous, and the Howship's lacunæ are wider and more irregular. As a result, the Haversian canals that are formed are abnormal. They are wide, irregular, and are enclosed by a bony wall of insufficient thickness and of most irregular shape. At the same time, the actual area over which the formation of bone is taking place is much greater than that which is observed in the normal growing bone.

The effects of these alterations in the formation and growth of the bone manifest themselves in the shape that the bone ultimately takes. Owing to the softness of the newly formed bone the bone itself yields to the various forces that are brought to bear upon it. Thus the tibia and fibula curve either outwards or forwards, leading to the different varieties of 'bow leg,' the femur curves forwards at its lower end or outwards at its upper end, the radius curves dorsally at its lower end, and so on. One of the most important results of rickets is seen in the alterations in shape undergone by the pelvis. Several distinct varieties of acquired malformation due to rickets are known, but the commonest as well as one of the most important is that which leads to the formation of the **flattened** pelvis. In this condition there is a smaller antero-posterior diameter of the brim of the pelvis due to the yielding of the pelvic bones during the growing period of life. This yielding is the combined result of the impaired nutrition of the bones which renders them more liable to be acted upon by outside forces, and of the pressure exerted upon them by the femora acting upwards and the weight of the spinal column acting downwards. The contracted pelves resulting from rickets become of vast importance in the case of the female, owing to the obstacles they interpose in the way of parturition.

Although the bone as it is laid down at the commencement of rickets is of a particularly spongy and soft character, a rickety bone when the individual has reached to adult life is not softer, but, on the contrary, harder and denser than normal. The alteration in shape which was impressed upon the bone when it was still soft, persists, of course, but the alteration in density is most marked. In such an adult bone, if a longitudinal section be made, it is always possible to see that there is a 'buttressing' of the bone on the inner side of the curve.

Scurvy rickets.—Under this name is designated a morbid condition affecting the bones which has certain resemblances with

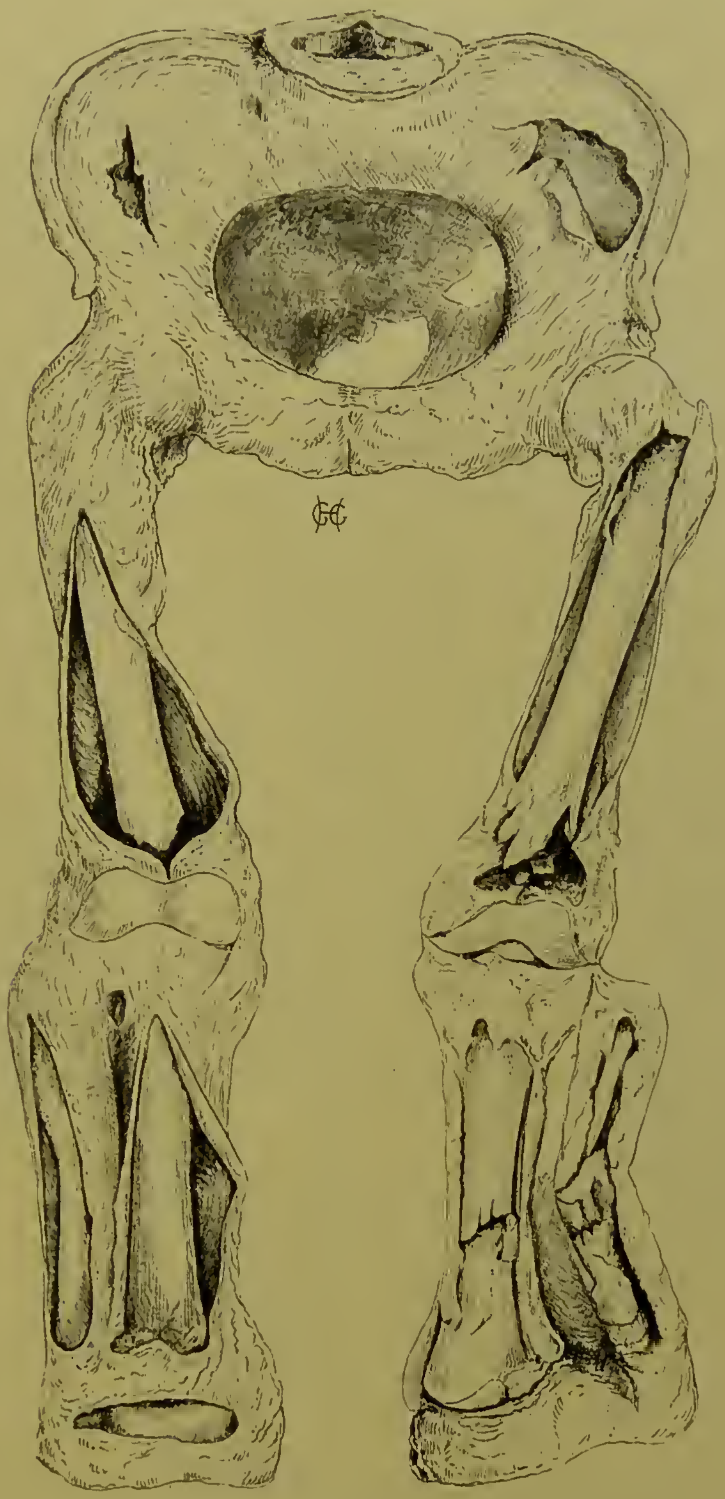


FIG. 84.—SCURVY RICKETS. × $\frac{2}{3}$.

The periosteum is thickened and loosely attached to the bones (particularly over those of the lower limbs), and the internal surface is dark from hæmorrhage. The shafts of the bones are short, the epiphyses thickened, and numerous fractures of the bones are present.

and certain differences from ordinary rickets. It affects infants under a year old as a rule, and is characterised by the facts that the bones which it affects are extremely liable to become fractured, and that sub-periosteal hæmorrhages are of practically constant occurrence. These hæmorrhages are particularly liable to occur in the highly vascular growing tissue at the ends of the shafts of the long bones and from thence pass beneath the periosteum and travel along it. Owing to the situation at which the hæmorrhages take place, it is common for separation to occur between the diaphyses and the epiphyses. Nevertheless definite fractures occur at other situations. These points are well shown in the accompanying figure.

Both rickets and scurvy rickets are general diseases, although the most characteristic manifestations are seen in the bones. Hence they are accompanied by changes in other tissues and organs. Thus it is characteristic of ordinary rickets that the spleen should be enlarged, and that the lungs should be particularly liable to the occurrence of various forms of inflammation, especially broncho-pneumonia. So, too, in scurvy rickets, the hæmorrhages are not confined to the periosteum, but are to be met with in the muscles, the subcutaneous connective tissue, and the mucous surfaces. Hæmaturia has also been observed in many cases.

As to the actual nature of scurvy rickets, and particularly its relation to ordinary rickets, there is a difference of opinion. Some authors maintain that the condition is a mixture of scurvy and rickets; others, that the disease is a separate entity, and is unrelated to either of them. The general tendency at the present day is to consider that the condition is one of severe rickets occurring in a child whose nutrition is so bad that it has become affected with scurvy.

The chronic osteoses. (*a*) **Osteitis deformans.**—Although it would appear from the name that has been given to this morbid condition of bone that it is a variety of inflammation, there are many reasons for believing that this is not the case. The name has, however, become so consecrated by usage that it is impossible to replace it by any other. This and the succeeding morbid processes of bone are closely allied to the group of chronic fibroses.

Osteitis deformans is a disease of old age, though it probably commences in middle life. It is of somewhat rare occurrence, but the changes undergone by the bones are so definite that the condition cannot well be mistaken for any other. It consists in an alteration of shape and density in the entire osseous system of the body, the bones becoming larger, heavier, and far more irregular in outline than normal. In the case of the tibia, for example, the thickness of the shaft may be doubled. In the majority of cases the bone is, at the same time, denser than

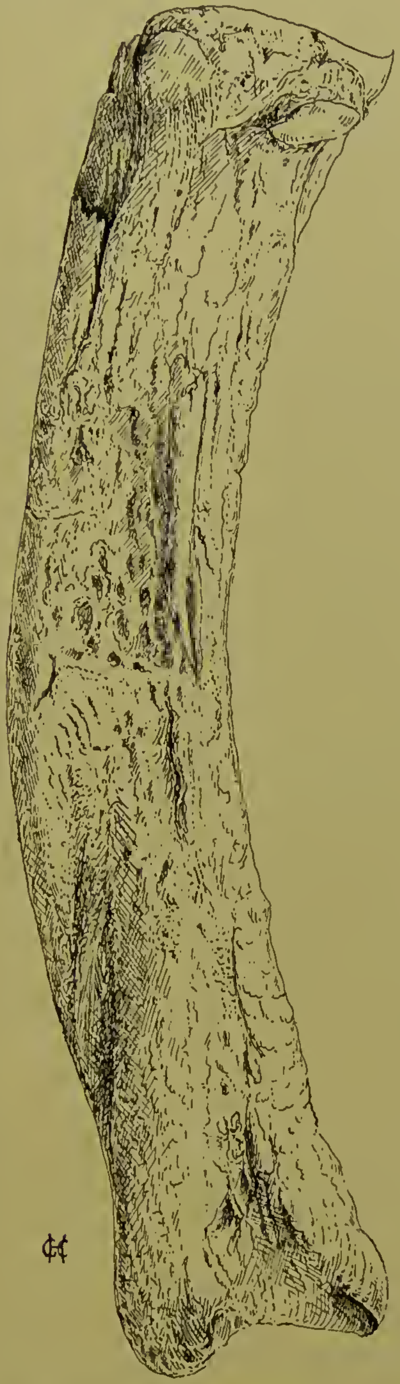


FIG. 85.—OSTEITIS DEFORMANS. OUTER SURFACE OF TIBIA. × $\frac{2}{3}$.

The bone is thick and very rugged, none of the normal surfaces for attachment of muscles being recognisable.

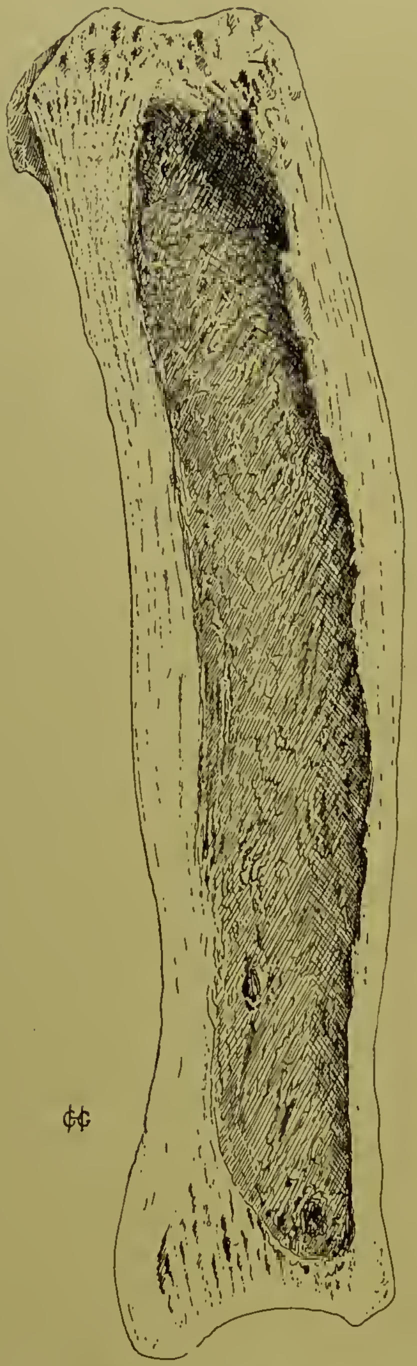


FIG. 86.—OSTEITIS DEFORMANS. INTERNAL ASPECT OF FIG. 85.

The medullary canal is rugged, there is little cancellous tissue at the ends of the bone, and the shaft is dense and enormously thickened.

normal, but in some cases the increase in size and weight is accompanied by a diminution in density. Frequently osteophytic outgrowths are present about the articular ends. Occasionally the condition does not affect the entire skeleton, but only one group of bones, or even only one bone.

The osseous change in cases of osteitis deformans proceeds, in most cases, both from the medullary and from the periosteal side, so that a diminution in the extent of the medullary canal in the long bones accompanies the increase in their size. A corresponding alteration takes place in the bones of the skull when they are affected, as is usually the case. For then there is entirely lost that division of the bones into an inner and an outer table and a diploë which is natural. The increase in the size of the skull is frequently sufficiently great to be recognisable during life.

A condition which is of fairly common occurrence in old persons, and which has certain relationships with osteitis deformans, is only seen on the post-mortem table. It is an alteration of the bodies of the vertebræ, particularly in the dorsal and lumbar regions, and consists in the formation of a number of osteophytes about the upper and lower surfaces of the bodies. Frequently the affected portion of the spinal column is rendered immobile by the formation of bridges of newly formed bone which pass from one free edge of the vertebra to the free edge of the vertebra immediately above or below it. These newly formed masses of bone are of considerable density. In addition to their having relationships with osteitis deformans, they also are related to the condition which we shall afterwards have to describe as arthritis deformans or rheumatoid arthritis.

(*b*) **Acromegaly.**—Under this name is designated a general condition of which the most manifest changes are an alteration in certain of the bones. The change consists in an increase in size, together with an increase in density of the bone, and generally a tendency to the formation of osteophytic outgrowths in the neighbourhood of the articulations. The bones affected are those of the head and face and those of the extremities. The changes in the size of the hands and feet are so remarkable as to be quite characteristic, and the same is true of the enlargement of the lower jaw. In advanced cases the change may be manifested over the entire skeleton. When this is the case it is difficult to distinguish acromegaly from osteitis deformans. An important point in the differentiation is the fact that acromegaly is a disease of young or of middle life; osteitis deformans a disease of advanced old age. So far as concerns the actual changes undergone by the bones, they are identical in the two diseases.

(*c*) **Leontiasis ossea.**—In this disease the characteristic change is an enormous increase in the size and the density of the bones of the face and skull; a skull in such a case may weigh ten pounds. The condition is one which is not well defined from the other conditions that have already been described in which the bones are enlarged. It is held by some that it is a localised manifestation of the changes which, when general, constitute gigantism. Certain other forms of chronic osteosis are known, but are so rare that we shall not delay to consider them here.

Deformities.—It is clear that a considerable number of deformities depend upon irregularities in the bones, but it is impossible to enter here into a description of all the different varieties of deformity that are known. Nevertheless a few words may be said about the general processes upon which deformities depend and the principal characters which they present.

Deformities may be either congenital or acquired. Amongst the congenital varieties we have all those which depend upon errors in development. A very large number of these concern the skull and vertebral column, and consist in a failure to close of those corresponding portions of bone which normally close to form a cavity or a canal. Thus we meet with cases in which the two halves of the occipital bone do not unite, with the result that the brain lies immediately beneath the scalp and only separated from it by the meninges. Similar failures to develop or to unite lead to a large variety of malformations of the skull. In the case of the face the principal malformations arise from the failure to unite of the two superior maxillæ and the præmaxilla, leading to the production of the various forms of harelip and cleft palate. In the case of the spinal column the chief deformity is that known as spina bifida, which depends upon a failure to close of the lateral processes which normally join together to form the dorsal arch of the spinal canal. A space is left in consequence which allows for the protrusion of the membranes of the cord, and a smaller or larger sac is formed which lies immediately beneath the skin, and is in direct communication with the sub-arachnoid space. The commonest situation in which a spina bifida is found is the sacral region; cervical spina bifida is known, but, apart from some severe malformation of the bones of the skull, it is excessively rare.

In the case of the extremities the most important deformities are those which constitute the different varieties of club-foot. Of these a large number are purely congenital, and are due to definite errors in development. Others are in a certain sense acquired. That is to say, they become manifest during the early years of the child's life, but are nevertheless primarily due to some slight defect in development. The chief factor in their progressive development is the lack of balance in the action of the muscles, owing to the structural peculiarities in the bones to which they are attached. From this it follows that a condition of club-foot commonly becomes aggravated as time goes on.

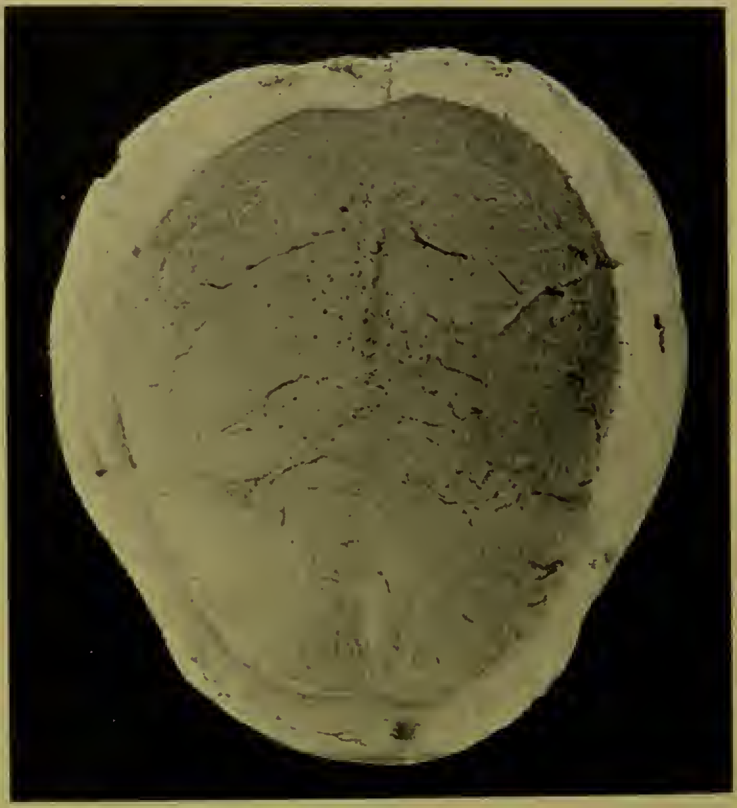


FIG. 87.—LEONTIASIS, VAULT OF SKULL.

The bone is enormously thickened and very dense; the diploë has disappeared. The dural surface of the bone is rugged, and the sulci for the blood-vessels are abnormally deep.

Besides those varieties of deformity which are definitely due to errors in development, there are others which are as definitely acquired. Thus, when the large multipolar cells in the anterior cornua of the cord have degenerated in the lumbar and sacral regions, and have led to a paralysis of the lower limb, it is not uncommon for a deformity to be produced in later years. This is due to the fact that the paralysis and atrophy of those muscles whose nutrition is controlled by the nerve cells in question have led to a lack of equilibrium so far as the muscular forces acting upon the limb are concerned. Since the disease in which these muscular and nervous changes occur is one which attacks children at an early age, it follows that the growing bones are subjected to an entirely abnormal distribution of forces. They therefore suffer in their development from this cause, and when it is remembered that the same causes persist during life, and are intensified by the increasing weight of the unaffected portions of the body, it is not unnatural that the ultimate condition of the affected limb should be one of marked distortion and deformity.

Upon the lines indicated in the last paragraph it is not difficult to understand that the deformities of the lower limb are more pronounced than those of the upper limb. As a matter of fact, in the case of the upper limb the deformity is usually confined to those changes which are dependent upon the improperly balanced action of muscles alone.

Other acquired deformities occur as the result of rickets. Reference has already been made to the curvatures of the long bones, and the alterations in shape of the pelvis and skull. It may be added that genu valgum or 'knock-knee' is also in many cases of rickety origin. But in some cases it is congenital, and due to an excessive size of the internal condyle of the femur. Coxa vara is another example of a deformity due to rickets.

(3) **New-growths.**—The new-growths of bones are both primary and secondary, but in the larger number of cases when a new growth is found in a bone it is primary.

Primary new-growths may be non-malignant or malignant. Of the non-malignant neoplasms the osteoma or exostosis is the commonest. It has very close relationships with those localised formations of new bone which occur in cases of chronic inflammation, and in the series of diseases which we have already described as chronic osteoses. In the latter cases the bony outgrowths are termed **osteophytes**, but there is really nothing except their mode of origin, and, to some degree, the situations in which they are most commonly found, which distinguishes them from true tumours of bone. In both cases they consist of bony tissue of great hardness in which the Haversian canals are few and very small. In the case of the skull, bony tumours are sometimes found to lie both on the outer and on the inner tables of the bones, which are of a density so intense that they are termed **ivory exostoses**. In this situation, as in others, there is a tendency for the bony tumours to be multiple.

The only other form of new-growth of a non-malignant nature which is liable to affect the bones is the chondroma. This form of growth is principally found in connection with the ends of the long bones, and particularly those of the hand. In spite of the fact that the tumours are composed of cartilage, they do not spring from the cartilages of the articulations, but from the ends of the shafts of the bones themselves. It is probable, as has been said elsewhere, that they originate in portions of cartilage which have remained concealed in the bone itself during the process of its formation.

The malignant tumours of bones are either sarcomata or carcinomata, the latter variety of growth being always secondary. Primary malignant tumours of bone are always sarcomatous, and any of the different varieties of sarcoma, with the exception of the melanotic sarcoma, may be found. The commonest are the spindle-cell and the myeloid-cell sarcomata.

It has already been said that we have to distinguish between those sarcomata of bone which originate in the centre and those which originate in connection with the periosteum. There is the greatest difference between these two varieties, not only from their clinical aspects, the periosteal sarcoma being far more malignant than the endosteal, but also in respect of the character of the changes which they produce in the bones which are affected by them, in their histological composition, and in the situations at which they are respectively most commonly found.

The periosteal sarcoma, which is almost always composed of spindle cells, either large or small, but which may also consist of round cells, is accompanied by a greater or less degree of new-formation of bone. This newly formed bone shows itself in the production of delicate spicules of bone connected with the outer surface of the bone in which the sarcoma is developing, and it may be present in so large an amount that the bone in the tumour becomes evident when we attempt to cut the tumour with a knife. On the other hand, it may be only slightly developed, and then it is impossible to recognise the existence of spicules until the bone with the tumour has been macerated. But, in addition to the new formation of bone upon the outer surface of the bone (and such a condition we might expect when we consider that it is the periosteum from which the tumour arises), an alteration takes place in the substance of the bone itself and in the medullary cavity. For the medullary canal of a long bone, for example, becomes completely filled with a newly formed bone of moderate density, which corresponds fairly well with the macroscopic limits of the periosteal growth. The ultimate result of these changes is that, when a longitudinal section is made of such a bone, the part corresponding to the seat of the tumour is found to be far more extensively altered than was apparent from an examination of the external surface alone. This is a point of the greatest importance in view of the fact that the periosteal sarcomata show a pronounced tendency to become generalised.

In the majority of cases the alteration in the character of the bone at the seat of the formation of a periosteal sarcoma is more one of disposition than one of density of bone. At the same time, although the actual density of the bone may be less than that of the normal shaft, this fact is in some measure compensated for by the greater mass of bone which is present. Hence we do not find in the case of the periosteal sarcomata that pronounced tendency to the occurrence of spontaneous fractures which we find in the case of

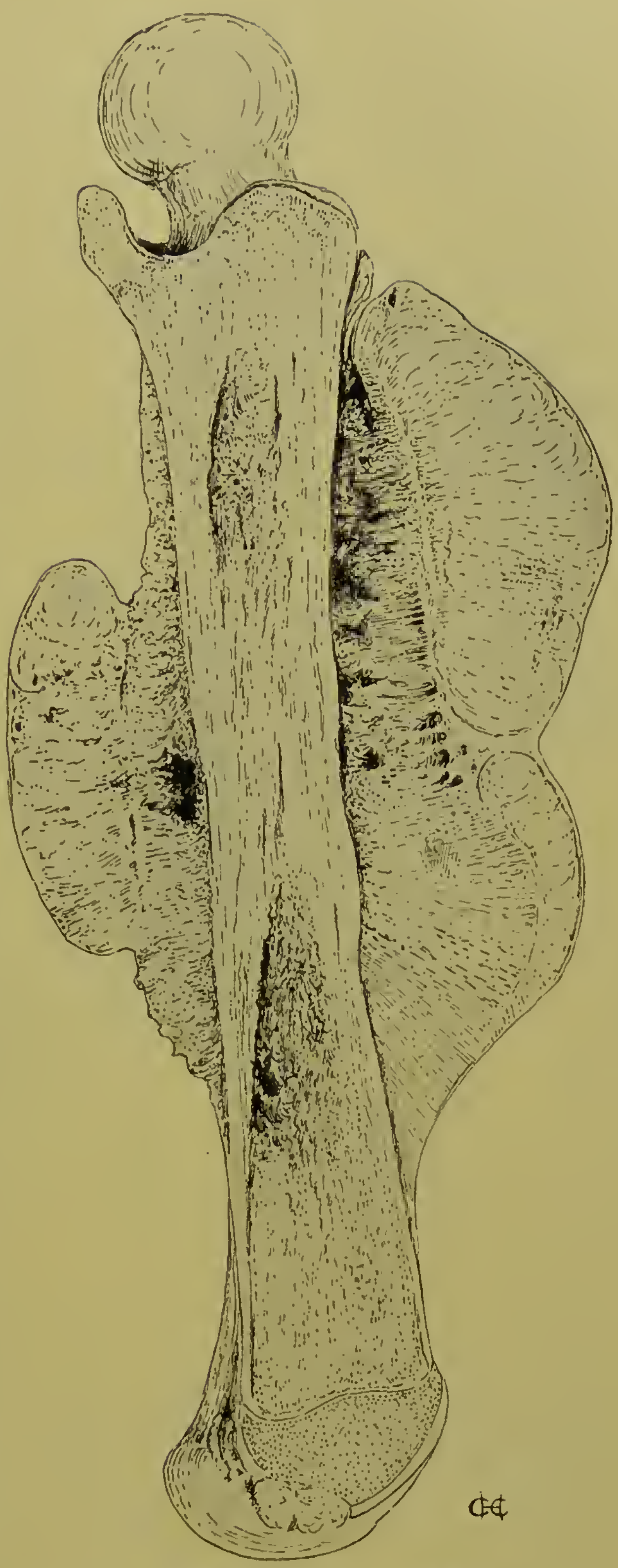


FIG. 88.—PERIOSTEAL SARCOMA OF FEMUR. × $\frac{2}{3}$. The growth is infiltrated with lines of calcification that extend into it from the bone as fairly parallel spicules. Though the growth is periosteal, note that it has invaded and filled a portion of the medullary canal.

the endosteal sarcomata. Nevertheless, in some cases such fractures do occur.

Of all bones which are liable to the occurrence of periosteal sarcomata, perhaps the femur is the most frequently affected. In it the growth is likely to show itself as a more or less unilateral swelling of the shaft; less commonly the growth surrounds the entire bone, and it may develop in connection with one of the extremities, probably the lower. Where sarcomata affect the short or flat bones, they are practically always periosteal. Such, for example, is the case when the bones of the pelvis are affected.

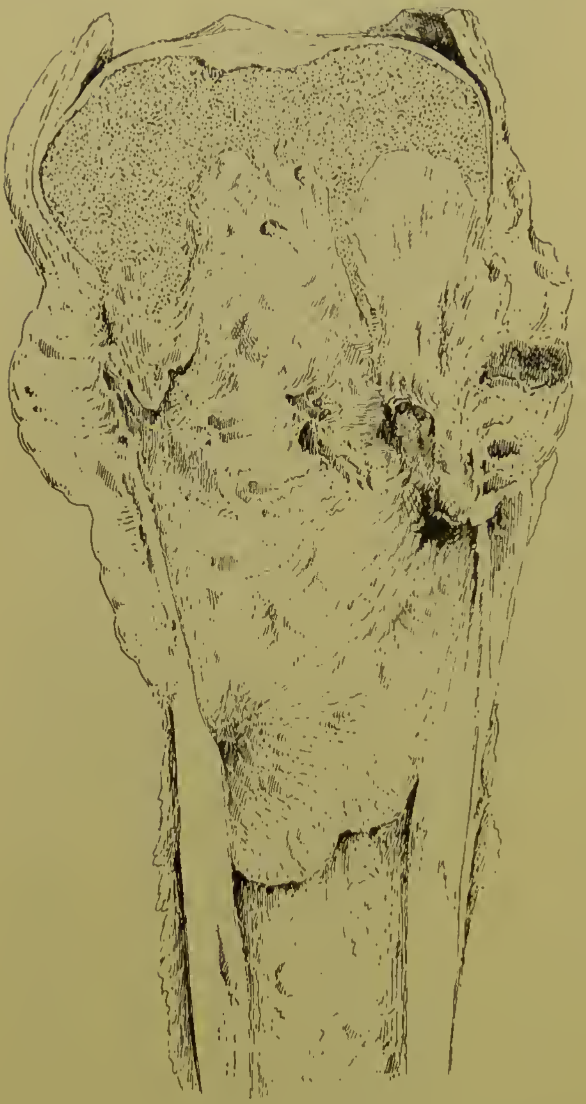


Fig. 89.—Endosteal Sarcoma of Tibia. × $\frac{2}{3}$. The growth lies almost entirely within the medullary canal and cancellous tissue of the head of the bone, causing extreme thinning of the corresponding portion of the shaft.

Endosteal sarcomata differ markedly from the periosteal in point of their much lower malignancy. They also differ in that they are generally of the myeloid type, and in that their growth is not accompanied by a new formation of bone, but, on the contrary, by a marked resorption of bone. For this reason fractures are particularly common, or rather, they would be particularly common were it not that the existence of the tumour is recognised by the surgeon, and the bone in which it is situated is removed before the destruction of the bony structure by the growth of the tumour has been carried sufficiently far for the occurrence of fracture to be inevitable. In a well-marked case the resorption is so considerable that when the bone is macerated a mere shell of osseous material—it is scarcely possible to speak of it as 'bone'—remains to mark the outer limit of the original tumour.

The endosteal sarcomata are most commonly found in connection with the lower end of the femur, the upper end of the tibia and of the fibula, the radius and ulna, humerus and upper jaw. A very common situation for the occurrence of endosteal sarcomata of the myeloid type is the jaw in connection with the fangs of the teeth. This condition, which forms one of the varieties of the disease known as **epulis**, does not differ from other varieties of endosteal sarcoma.

Chondro-sarcomata and osteo-chondro-sarcomata are of far less frequent occurrence than the varieties which have been mentioned above. They are generally found in connection with the ends of the long bones.

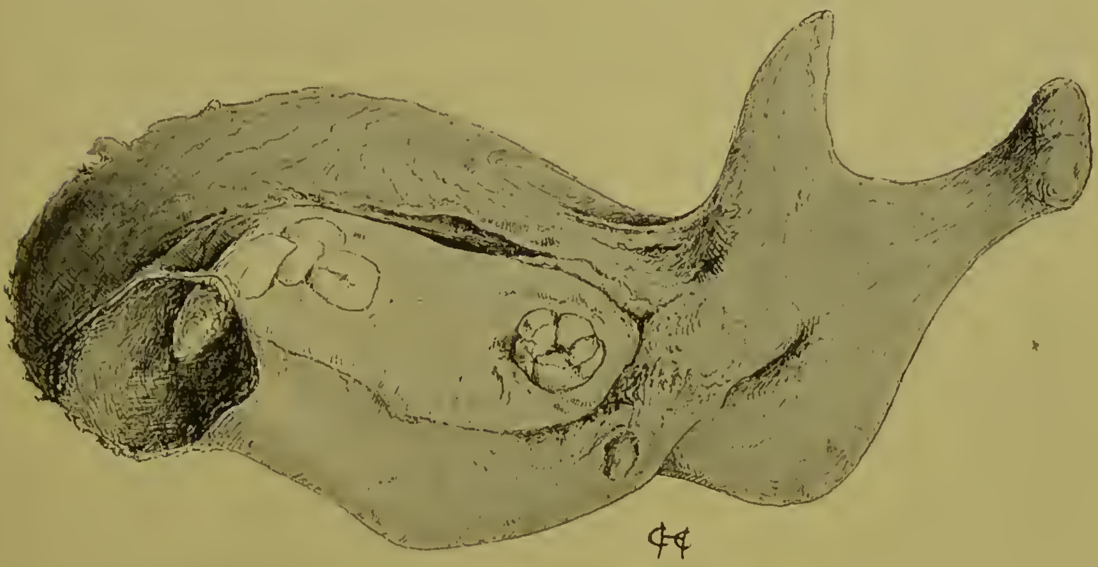


Fig. 90.—Myeloid (Endosteal) Sarcoma of Lower Jaw. Natural Size.

The growth has caused great expansion and deformity of the bone.

Secondary new-growths of bone may be either sarcomatous or carcinomatous. When sarcomatous, they may have originated in connection with a primary sarcoma of bone or of any other tissue, though the latter is rare. In the case of secondary carcinomata of bone, it is commonest for the primary growth to have been one of the breast. The reason for this lies partly in the fact that, of all forms of carcinoma, that affecting the breast is actually the most common, and partly in the close anatomical relations of the breast to parts of the skeleton. Nevertheless, in carcinoma of the breast it is not only the ribs and sternum which are liable to be affected by an extension from the primary growth, but also bones at a distance, such as the humerus.

When a secondary growth takes place in a bone, it is unaccompanied by any new formation of bone. On the contrary, its growth is directly associated with an absorption of the pre-existing bone. Hence in such cases fractures are very common. Moreover, it is usual for the fracture to be the first indication that there is anything wrong with the bone, if we except the fact that severe pain is sometimes felt at the seat of the formation of the secondary growth for some time previous to the occurrence of the fracture. Microscopical examination of the tissue composing a secondary nodule reveals that the tissue is of the same nature as that in the primary growth, only far more cellular. In the centre of the nodule no indication whatever is found that the tissue in which the nodule was formed was bone. At the periphery of the nodule, however, portions of bone undergoing absorption are found, and into the lacunæ which are present finger-like processes of the new-growth itself, composed entirely of cells, are found. It is by reason of the pressure atrophy which these processes of the growth induce that the resorption of the bone is brought about.

Cysts of bones and the occurrence in them of animal parasites are so rare that they need not detain us here.

SECTION VI

THE JOINTS, MUSCLES, TENDONS, AND BURSÆ

Before proceeding to consider the changes which affect the joints a very few words may be said as to the morbid changes undergone by cartilage itself, so far as it is not concerned in the formation of a joint.

The commonest change of cartilage is **calcification**. This, which is always present to a greater or less extent in the costal and laryngeal cartilages of the aged, may be even described as a physiological, as distinguished from a pathological, change. The calcareous particles are deposited quite irregularly in the cartilage, and may be present in so large an amount that it is impossible to divide the cartilage with a knife. Actual **necrosis** of cartilage may be seen in the case of the arytænoids in typhoid fever and in similar debilitating diseases. Disappearance of cartilage as the result of pressure atrophy occurs in cases of aneurysm and solid tumours. **Fractures**, as has already been said, may occur, and then repair by the formation either of new bone or of fibrous tissue, but never by new formation of cartilage.

With these exceptions, the most important changes to which cartilage is liable are those which affect it secondarily after commencing in the perichondrium. Thus necrosis of the arytænoid cartilages in typhoid fever commences in a perichondritis, and it is this inflammation of the perichondrium which interferes with the blood supply of the cartilage itself to a sufficient degree to lead to the necrosis. The same is true when the cartilages of the larynx are affected in tuberculosis, syphilis, and leprosy.

Another variety of chondritis and perichondritis is that which occurs in connection with congenital syphilis. It concerns particularly the ossifying cartilages at the junction of the diaphyses and the epiphyses of the long bones, and accounts for many of the bone changes present in congenital syphilis. The exact change consists in an irregularity in the processes of calcification, so that foci are found at which there is a poor deposition of calcium salts or no deposition at all, and these are set side by side with foci at which the calcification is excessive. Besides the cartilage at the line of ossification, the cartilages entering into the composition of the joints are also similarly affected.

In the case of the cartilaginous rings of the trachea and bronchi irregular calcareous depositions are not infrequently found which extend for some distance and lead to an immobility of the tube. So far as is known, this change has no clinical significance, but it is probably comparable, pathologically, with the formation of calcareous plates in the aorta and great vessels. It is only met with in advanced life.

(1) THE JOINTS

The pathological changes undergone by the joints are of the most diverse nature, but the actual processes at work are, in the main, similar to those which lead to the morbid changes in bone. We find, therefore, acute and chronic inflammations, chronic changes which are not definitely inflammatory (chronic arthroses) and the various effects of injury, all of which subsequently become modified by the occurrence of inflammation.

(1) **Acute inflammations.**—Undoubtedly the most important acute inflammations of joints are the rheumatic, the gouty, and the pyæmic. Each of these merits separate attention.

(*a*) **Rheumatism.**—The rheumatic affections of joints show themselves under two forms, the acute and the chronic. In acute rheumatism the joint is acutely painful, red, swollen, and hot, so that it manifests in a typical degree the cardinal signs of inflammation. In the few cases in which it is possible to inspect the interior of the joint, it is seen that the synovial fringes are injected and swollen, that there is an excess of synovia, and, sometimes, that particles of fibrin are floating in the synovia. Acute though the inflammation undoubtedly is, it is commonly of very short duration, one of the most marked features of the disease being the rapidity with which the inflammation attacks a given joint, and as suddenly leaves it to attack another. Since the process recedes very rapidly from a joint in which it was a little earlier most intense, the changes found in the joints at an autopsy on a case which has died of acute rheumatism are most meagre.

In chronic rheumatism the entire process is slower in its course, and the anatomical changes found upon examination of an affected joint are greater. In such a case it will be found that the surfaces of the cartilage are no longer smooth, but that they show the presence of tags of fibrin, and not infrequently the presence of definite fibrous adhesions which pass between the surfaces of the joint, and more or less impair its mobility. Sometimes, indeed, the joint is rendered completely useless.

Now this formation of adhesions would not have taken place had it not been that the cartilage of the joint had become destroyed in whole or in part. That this is the case is readily recognisable in a frankly chronic rheumatism, for a joint from such a form of the disease either shows that there is an entire absence of cartilage, or, more commonly, that foci with irregular edges are present, and that those portions of the articulating surfaces of the bones which are denuded of cartilage are covered by a dense fibrous tissue. This denudation of cartilage principally affects the centres of the articulations; around the edges the cartilage may be found to be relatively intact. By forcibly breaking down the adhesions, the mobility of the joint may in many instances be largely restored. Such forcible movement, however, is bound to light up a fresh inflammation in the joint, and must only be resorted to after mature consideration.

The variety of chronic rheumatism which has just been described is one which arises in an attack which was at the first either definitely acute or subacute, and the passage from the one state to the other is marked by no distinct limit. Another variety is known which does not originate in an acute attack, but which appears to be chronic throughout. It is seen in a characteristic form in the case of agricultural labourers, omnibus drivers, and similar persons whose work causes them to be exposed to all kinds of weather.

This variety of chronic rheumatism has marked differences from acute rheumatism, and at the same time has many resemblances to the condition which we shall subsequently describe as arthritis deformans. Thus whereas it is characteristic of the acute form that it generally tends to affect the large joints, such as the knee and the shoulder, it is characteristic of the chronic variety now under consideration that it tends to affect the small joints, particularly those of the hands. In arthritis deformans both large and small joints are affected. Then, too, in the case of acute rheumatism the tendency to the permanent alteration of an affected joint is small; as a rule, when the acute inflammation has passed away, the joint returns to an absolutely normal condition. But in the chronic rheumatism due to exposure, the joints become enlarged and stiff, owing to a general enlargement of the ends of the bones, and a rigidity of the ligaments and tendons connected with them. There is an absence, however, of those alterations in the cartilages which are characteristic of arthritis deformans, although enlargement of the ends of the bones in the immediate neighbourhood of the joints is a constant feature of the latter disease. But one of the most marked differences between this chronic variety of rheumatism and that which arises out of an acute or subacute attack is that the chronic rheumatism of exposure is of very insidious onset. In this respect it has great resemblance to arthritis deformans.

It is quite possible that we shall ultimately have to separate chronic rheumatism due to exposure from true rheumatism. There is much evidence that the acute form of rheumatism—rheumatic fever—is an acute infective disease of bacterial origin. Quite recently a number of cases have been found to be directly associated with the presence of a variety of diplococcus, having somewhat distinctive characters. And although it is highly probable that acute rheumatism is due to a micro-organism, and, therefore, that that variety of chronic rheumatism which arises out of the acute form is also bacterial, it is by no means clear that 'rheumatism' due to exposure comes into the same category. The fact is that we are somewhat accustomed to regard any condition which is closely associated with cold, and which manifests as its principal symptom a painful enlargement of joints, as a form of rheumatism. It is quite possible that the joint affection from exposure is nothing more than a simple chronic inflammation of the joints in which cold is the irritant. It would be well in accord with this view that a local increase obtains in the amount of the different members of the connective-tissue group present.

(*b*) **Gout.**—In gout the characteristic change is a deposition of a white mortar-like substance upon the surfaces of the affected joints. Viewed macroscopically, this white substance looks as if it were simply laid on the surface of the cartilage, but when an attempt is made to remove it, it is seen that the connection between the substance and the cartilage is very intimate. Microscopically, the white substance resolves itself into a deep meshwork of delicate needles (sodium biurate) which lie in the actual substance of the cartilage of the joint. In spite of their apparently superficial position, it is only in very advanced cases that the meshwork of needles fails to be covered by a thin layer of cartilage. In an early stage of the disease the white deposit is only found in the centre of the cartilage, but when the disease is advanced the appearance suggests that the white material has been laid over the entire cartilaginous surface of the joint with a brush. In such an advanced case, too, it is likely that a similar deposit will be found in the ligaments of the joint, though, probably, not to the same extent.

Gout is an affection in which the small joints are particularly involved. It is only rarely that the large joints become affected, and even then it is rare for them to become definitely inflamed, unless numerous attacks have previously occurred in the small joints. Of all articulations the metatarso-phalangeal joint of the great toe is that most frequently affected. Usually it is the first joint attacked, and even if this be not the case, it is in the highest degree rare for it to remain unaffected throughout. Although the larger joints may not become definitely the seat of inflammation during the patient's life, it is common to find, after death, that a small deposit of the salt has taken place in them. Quite a considerable deposit may be found in the knee-joint, for example, without there being any history of an attack in this part.

Although it is commonest for the crystals of sodium biurate to be deposited in the articular cartilages, in marked cases they become deposited outside the joints altogether. Even then we find them in connection with the denser forms of connective tissue such as tendon and cartilage. Thus 'chalk stones' are local accumulations of the crystals in the immediate neighbourhood of the joints and actually in the sheaths of the tendons which pass over them. And the 'tophi' which are found on the helices of the ears in gouty persons are local deposits of sodium biurate on the cartilage of the pinna of the ear. In both these instances the accumulation of the salt forms a hard mortar-like substance in the fully developed case, but at the commencement the deposited material is soft and creamy in consistence. This is a matter of some importance, for there is thus produced a local swelling which is soft and may give fluctuation, and since the actual attack of gout is accompanied by a rise of temperature, it may be mistaken for an abscess. The formation of a definite chalk stone is a matter of time, and is brought about by the absorption of the liquid which accompanied the first deposition of the crystals.

Although it is commonest for the articulations of the feet to be affected in gout, chalk stones are most frequently met with on the hands about the knuckles. Owing to the interference with the nutrition of the skin which they produce, and their exposure to injury, the skin over chalk stones is liable to ulcerate. When this has occurred, portions of the deposited substance readily break away.

(*c*) **Pyæmic inflammations.**—In its most characteristic form when pyæmia leads to the affection of a joint, it induces an intense suppurative disorganisation. On opening the joint the cavity is filled with pure creamy pus, the ligaments are softened and may be ulcerated through, the synovial fringes are red and œdematous, and the cartilages themselves may be ulcerated in places or entirely loosened. It is not always that so severe a condition is observed, however, owing to the pain which the inflammation of the joint induces, and the interposition of the surgeon before matters have proceeded to this extreme. In most cases when the joint is opened surgically the cartilages are not detached, and the ligaments are not, although soft and red, completely ulcerated through. But it is almost certain that the cavity of the joint will be found full of pus, and although the articular cartilages do not *appear* to be irretrievably damaged, this is none the less the case. For a joint which has once been the seat of pyæmic inflammation has invariably lost its function, and recovery can only take place along with a disappearance of the structure of the joint and its replacement by a mass of newly formed fibrous tissue which renders the formerly moveable joint completely stiff. Into the processes which lead up to this condition it is unnecessary to enter, since they can easily be understood by applying the general principles discussed along with the pathological sequels of inflammation and repair. It has only to be remembered that in pyæmia the irritant is a highly virulent pyogenetic micro-organism.

A somewhat special form of pyæmic inflammation of the joints is presented by the condition known as gonorrheal rheumatism. When gonorrhœa has lasted for some time, and has passed into a condition of a chronic gleet, it is not very uncommon for the patient to be attacked by pain in the left knee joint. Why it is that this joint is the one which is most frequently affected it is impossible to say, any more than why the great toe joint shows a special liability to become affected in gout. The gonorrhœal affection manifests itself as a painful swelling of the joint with some stiffness. As a rule suppuration does not occur, neither is there a tendency for many joints to be affected, but sometimes the condition becomes very severe, and then there is nothing to distinguish the disease from ordinary pyæmia. As to the nature of the condition, there is little doubt that it is a mild form of pyæmia, the more so as we know that a definite pyæmia may originate in a gonorrhœa and present all the classical symptoms, including an ulcerative endocarditis.

In the acute stage of gonorrhœa a condition similar to the more severe form of that joint affection which has been described in the last paragraph is sometimes seen. It then comes on three or four days after the urethral discharge has become established, and is undoubtedly pyæmic.

Before leaving the acute inflammations it will be convenient to mention the simple forms of arthritis which depend upon injury. In these the alteration of the joint is, in the less severe cases, one in which there is an effusion of fluid into the cavity which distends it and impairs its movement. In the largest number of cases the fluid poured out is clear and contains no fibrin flakes. But in more severe cases the fluid contains red blood corpuscles or may even practically consist of pure blood, and fibrin flakes or actual blood clot may be present. The ultimate changes which are undergone by the joint depend upon the degree of injury to which it has been subjected. Fortunately in most cases a process of resolution takes place, and the joint becomes after a time as good as ever. But in other cases the inflammation which results from the initial injury, coupled with the irritant action of the blood &c. which is poured out, leads to the formation of definite adhesions and a corresponding impairment of the usefulness of the joint.

(2) **Chronic inflammations.**—The most important of the chronic inflammations of joints is the tuberculous. Indeed, of all diseases of joints tuberculosis is that one which we meet with most commonly in the practice of a hospital. The other infective and chronic inflammations affect joints so rarely that they need not detain us; syphilis, in particular, in spite of the diversity of the structures which it is liable to attack, hardly ever is a cause of articular affection.

Tuberculosis of joints may arise in two ways. Either it may commence in the bone in the neighbourhood of the joint and invade the joint itself secondarily by extension of the process, or else it may commence in the synovial membrane of the joint itself. It is difficult to say which of these two methods is the more common; probably a difference obtains in the case of different joints.

Any articulation may be affected by tuberculosis, but the disease is most common in the hip joint, the ankle, the joints of the tarsus and the knee. Then follow the joints of the upper limb, but tuberculosis is more common in the elbow than at either the wrist or the shoulder. Then follow the articulations of the vertebral column, particularly those in the cervical region and the occipito-atlantoid. Such disease of the articulations is far less common than the tuberculous disease of the bodies of the vertebræ which has already received attention. Although it can hardly be considered an articulation in the same sense as those to which reference has been made, it must be added that the sacro-iliac synchondrosis is somewhat liable to be affected by tuberculosis.

In all these cases the actual changes which are produced are very similar, differing only according as the tuberculosis attacks the joint primarily or secondarily to an antecedent disease of bone. Where the disease affects the joint by extension it is uncertain at what point the articular cartilages of the joint first become attacked ; this depends upon the point at which the disease in the bone is situated, upon the density of the bone lying immediately beneath the cartilage and other factors of a like nature. But when the disease affects the joint primarily it extends to the cartilages from the periphery. For in such cases the disease always commences in the synovial membrane of the articulation.

The earliest change that is visible, therefore, in a case of a primarily articular tuberculous disease of a joint consists in a swelling of the synovial fringes due to the deposition in them of a greater or smaller number of anatomical tubercles. These tubercles are not recognisable macroscopically, but they lead to the formation of a mass of granulation tissue which replaces the synovial fringes. At the same time that this granulation tissue is being formed the articular cartilages are undergoing absorption, and since the granulomatous change of the synovial fringes extends into the joint from the periphery, the disappearance of the cartilages takes a similar course. When the process has once destroyed a portion of the articular cartilage, it readily proceeds to invade the underlying bone and to induce caries.

In some instances the tuberculous material shows its normal tendency to undergo caseation, but in others this process is not manifest. Hence we find three somewhat distinct macroscopic pictures of tuberculous disease of joints. In the first, which may be taken as the type, there is present a mass of pink granulation tissue which has a peculiar gelatinous appearance, and this corresponds to a greatly increased area of the normal synovial fringe. Internally to this gelatinous material comes a narrow zone with somewhat irregular margin, which is bright pink in colour and corresponds to the thinned edge of the articular cartilage. More internally comes a larger or smaller layer of cartilage which differs in no obvious respect from the normal, being white and glistening. In the second variety of tuberculous disease of joints the formation of a gelatinous material from the synovial fringes has dominated the whole process, and we find that little more is visible than that the entire joint cavity is filled by a slightly pink gelatinous material. Nevertheless the ligaments of the joint are softened, and in some cases definitely ulcerated, and the cartilages, although they may not show as much change as in other cases, are softened to such a degree that in a very little time they would have undergone complete disintegration. In the third variety the dominating feature is caries. The soft portions of the joint are ulcerated with rapidity, and the articular surfaces of the bones soon become more or less completely destroyed by the inflammation. In this variety the caseous degeneration of tuberculous material is more in evidence than in either of the two other varieties. Caseation is probably mixed up with true pus formation, but nevertheless the purulent material formed in the cavity of the joint is curdy, and has the characters of the pus of a cold abscess rather than those of an acute abscess.

When repair of a tuberculous joint takes place, it is clear that there can be no regeneration of the destroyed cartilage. Hence repair is always accompanied by the formation of fibrous adhesions and a stiff joint.

Owing to the pain which is associated with tuberculous disease of the joints, and the internal pressure which is produced in them by the accumulation of the products of the inflammation, the patient places the limb in the position in which it is easiest. This is in most instances a position midway between extreme flexion and extreme extension. At the same time when the ligaments of the joint have become softened, and still more when they have been destroyed, the position of the limb is determined largely by its own weight. If, then, repair takes place, the limb becomes fixed in a position determined by these factors. Hence tuberculous disease of joints is an important factor in the production of deformities.

In the case of the joints, as in the case of other tissues, tuberculosis is a disease of youth. But, though the patients affected are generally at or about the age of puberty when they first come under notice, a certain number are first affected in old age. There is thus a definite senile tuberculosis of joints. In this variety the process is much more chronic and indolent, so that it is for a long time difficult to determine whether there is, or is not, any distinct disease of the joint. For the same reason when the disease has definitely declared itself the changes to which it gives rise are less marked than the changes affecting the same joint in youth. There is a superficial caries of the bones, a little suppuration, and it may be one or two sinuses are formed. As might be expected, when tuberculosis affects joints in old age it is even more intractable than in youth.

(3) **Chronic arthroses.**—It must be clearly understood at the very commencement of our discussion of these affections that, although there is a considerable amount of reason for their separation from the chronic inflammatory lesions of joints, yet it is not completely certain that we are justified in separating them off from the inflammations as we are here doing. The reasons for and against the present arrangement will appear as we proceed.

The articular diseases that we have to consider are two in number, viz. arthritis deformans and Charcot's disease.

(*a*) **Arthritis deformans.**—In this disease there occurs a profound alteration of the entire joint, including the articular surfaces of the bones entering into its composition. Sometimes one joint alone is affected, but more commonly several are diseased, and in marked cases there is hardly a joint in the whole body which is completely unaffected.

In the fully established disease observed, for example, in the knee joint, it is seen that the articular cartilages have completely disappeared, that the articular surfaces of the bones have become altered in density and show numerous ridges, that the articular surface lies lower, relatively to the edges of the joint, than normal, and that numerous osteophytes are present around the articular ends of the bones. The alteration of the articular ends of the bones is peculiar to this disease. Although the cartilages are completely absent, the parts entering into the composition of the joint have a polished appearance owing to the density and smoothness of the altered ends of the bones. This condition is known as **eburnation,** and it is brought about by the constant pressure and friction to which the ends of the bones are perforce exposed once the articular cartilages have disappeared. These same factors account for the ridges on the articular surfaces of the bones. These ridges correspond to one another, so that a ridge upon the lower end of the femur fits into, and during the movements of the joint travels along, a corresponding sulcus on the head of the tibia.

In spite of the profound alteration of the joint, there is, in an advanced case such as that which has been described above, no sign of the actual processes which led to the destruction of the articular cartilages, processes which it might be supposed would not have ceased without inducing some caries of the bones themselves. On the contrary, the entire process seems to be one of a slow atrophy combined with a sclerosis of the remaining bone and a new formation of bone in the immediate neighbourhood of the part chiefly affected. Nevertheless, if we examine a case at an earlier stage it becomes clear that at one time the process was far more acute than might have been expected from an examination of the terminal condition alone.

In a joint which is seen at an early stage the cartilages have an appearance which has been compared to pink velvet. The velvety change is brought about owing to the occurrence of a fibrillation of the matrix of the cartilage. Owing to the greater softness which accompanies this alteration, the friction due to movement readily leads to erosion, and ultimately to complete destruction of the cartilage. At the same time this process is aided by the alterations which take place in the synovial membrane.

The synovial membrane becomes congested, and the actual size of the processes constituting the fringe increases, so that the altered membrane comes to occupy a larger amount of space in the joint than normal, and, in particular, spreads over the articular surfaces. This alteration of the synovial membrane leads to the formation of a material which has marked resemblances with granulation tissue. Indeed, by many authors it is definitely so regarded. In any case its encroachment into the joint lasts only for a limited period, and when the destruction of the articular cartilages has been completed, nothing of the synovial membrane is left within the joint.

Even at so early a stage as that which has just been described, alterations have been taking place around the joint with the production of that 'lipping' which has been mentioned as characteristic, and the formation of numerous osteophytes. These changes we can only ascribe to the hyper-activity of the periosteal cells. It must be mentioned, however, that some authors hold that the new bone which is formed at the edges of the disappearing articular cartilages is formed from cartilage direct, and not from the periosteum.

The actual disease which we have now under consideration is known by several names, and this fact tacitly implies that its exact nature is uncertain. Thus the names 'chronic rheumatic arthritis,' 'rheumatoid arthritis,' and 'rheumatic gout' are evidences that the relation of the condition to rheumatism and gout is by some authors taken for granted. Of these terms, 'rheumatoid arthritis' is the least objectionable, if we do not choose 'arthritis deformans,' for at least it only suggests a similarity. Some authors apply the name 'arthritis deformans' to the terminal condition in which the cartilages have disappeared, and reserve their opinion as to whether this condition is, or is not, a late stage in the disease of 'rheumatoid arthritis,' by which they indicate the earlier stage which we have described. Nevertheless even these authors allow that the later stages of their 'rheumatoid arthritis' present appearances which are indistinguishable from our 'arthritis deformans.'

The question is further complicated by the fact that certain authors claim to have isolated from joints which were the seat of 'rheumatoid arthritis' a variety of micro-organism which they say is peculiar to the disease. If this is so, the micro-organism in question may be either accidental or causal. In the latter instance it is clear that we shall have to include the condition among the true chronic inflammations. That the cause of acute articular rheumatism is also the cause of arthritis deformans, is a possibility which at once rises to the mind, but so far there is nothing to support the view. Indeed, many authors are inclined to believe that the originating cause of arthritis deformans is to be sought in some alteration in the nervous control of the tissues of the joint. They base this view upon the analogy of Charcot's disease of joints, and, for them, any micro-organisms which may have been found are accidental.

Arthritis deformans is the cause of very marked deformities. Not only are the affected joints themselves larger than normal, but also the alteration of the tissues around the joints, and the tendency to the formation of fibrous adhesions within and around them, lead to the occurrence of persistent flexures and distortions. This change is often seen to a marked extent in the hand, where the distortion is very characteristic. Owing to the presence of numerous osteophytes, the joints are larger than normal, and the shapes of the articular surfaces are always altered in such a way that there is produced an inclination of the fingers to the ulnar side. At the same time the phalanges are almost always somewhat flexed.

When the fingers are affected, the skin which covers them becomes tight and shiny. It is doubtful how far this condition depends upon the uselessness of the hand—how far, that is, it is an atrophy from disuse. In this connection, and in connection with the whole question of the ætiology of the chronic arthroses, it is important to remember that a similar alteration of the skin is one of the most pronounced changes following upon severance of nerves.

(*b*) **Charcot's disease of joints.**—This condition is particularly seen in conjunction with the disease known as tabes dorsalis or locomotor ataxy, a disease in which one of the principal changes is a sclerosis of the posterior columns of the spinal cord. In many respects it resembles arthritis deformans, but in many it is completely different.

Charcot's disease is especially liable to affect the knee joint. It leads to a complete disorganisation of the joint, with a destruction of the cartilages, ligaments, synovial membrane, and surrounding structures. Hence the joint does not manifest that increase of rigidity which is characteristic of arthritis deformans, but, on the contrary, is abnormally mobile. At the same time, owing to the accumulation of the products of disintegration of the joint and the articular ends of the bones, the modification of the tissues around the joint by the absorption of fluid, and, probably, the entry to some degree of inflammatory products into the question, there is produced a considerable enlargement in the region of the joint.

The disease is one into which formative processes enter to a minimal extent. On the other hand, destruction proceeds with great rapidity. So far as the actual changes are concerned that lead up to the ultimate condition, they are similar to those which we have already described as forming the early stage of arthritis deformans. But they come on with far more rapidity, so that the entire knee joint may be completely disorganised within a few days in a severe case. The changes are not, however, always so rapid and extensive ; a gradual disintegration of the joint may take place which is unaccompanied by great swelling, and which may be months in progress. In any case the bones become worn down after the disappearance of the cartilages, and their surfaces towards the cavity of the joint become definitely concave. There is, therefore, an apparent resemblance to the 'lipping' of the bones in arthritis deformans, but a new formation of bone, including a formation of osteophytes, does not occur.

Loose bodies.—In many of the chronic changes which affect joints, loose bodies are found in the joint cavities. These bodies are usually somewhat flattened, have smooth outlines, and are of a cartilaginous hardness. They may be present in quite small numbers or may be very numerous, and though they are sometimes larger, they are usually less in size than a pea.

These bodies differ in different cases in their composition. As a rule they consist of a dense fibrous tissue which presents evidence that it is of inflammatory origin; that is to say, they are composed of a somewhat cellular fibrous tissue the fibrils of which are arranged irregularly. In other cases they consist of a centre of cartilage surrounded by a thinner or thicker layer of fibrous tissue, while in a very few instances they consist in part of bone. In all cases, however, they are completely avascular.

As to the origin of these loose bodies there is considerable doubt. In the case of those into the composition of which either cartilage or bone enters, there can be little doubt that they have originated from portions of the bone or of the articular cartilage which have become detached and have been rounded off in process of time. In the case of those which are composed of fibrous tissue, it may be that they are derived from portions of fibrin which had been deposited in the joint during the period of its active inflammation, or it may be that they are detached portions of the fringes of the synovial membrane. The latter explanation is probably the true one in a very large number of cases, and especially in those diseases such as arthritis deformans in which we know that the conversion of the synovial membrane into a mass of granulation tissue is a prominent feature. There can be no doubt that loose bodies, when they are present in a joint, play an important part in protracting the inflammation.

(2) THE MUSCLES

Although the muscles are extremely liable to be involved secondarily in a number of pathological processes, they are themselves subject to few primary diseases.

(1) **Atrophy.**—It is unnecessary to repeat here what has already been said as to the importance of this process. All varieties of atrophy may be witnessed in the case of muscle. Concerning that disease, however, in which the most pronounced atrophy is observed—progressive muscular atrophy—a word may be said. The disease in question is especially apt to affect the muscles of the upper limb, commencing, as a rule, in the interossei and extending gradually up the muscles of the forearm, the arm, and the shoulder to those of the trunk.

The actual changes which occur in the muscles in progressive muscular atrophy differ considerably in different cases. Thus in the same muscle we may find bundles that are completely atrophied side by side with others which appear to be fairly normal. In a case which has proceeded to an extreme, however, the entire muscle becomes converted into a mass of fibrous tissue, and gives no evidence at all, on microscopic examination, of the former presence of muscular tissue.

So far as the alterations in the muscle bundles are concerned, progressive muscular atrophy bears close resemblances to the disease known as pseudo-hypertrophic muscular paralysis. In the latter disease there is a progressive atrophy of certain muscles, notably those of the calf, the gluteal region, and the lumbar region, and, so far as the muscular change itself is concerned, the atrophy in the two cases is similar. But a difference is imported by the fact that in pseudo-hypertrophic muscular paralysis there is a definite increase in the amount of connective tissue between the muscular bundles, and in progressive muscular atrophy this is not the case. Moreover there is, in the pseudo-hypertrophic variety, a much more extensive conversion of the various tissues into fat. In progressive muscular atrophy such a fatty degeneration of the actual muscle and accumulation of fat globules in the connective tissue between the bundles does occur, but it is always far less marked, and in many instances appears to be absent altogether. An increase in the numbers of the nuclei of the connective-tissue framework of the affected muscles is observable in the case of both diseases.

Reference has already been made to the existence of fibrosis in the myocardium and to the atrophy of the heart muscle by which it is accompanied. In rare instances a somewhat similar fibrosis may be seen in other muscles. Its relation to the forms of fibrosis that occur in progressive muscular atrophy and in pseudo-hypertrophic muscular paralysis is uncertain, but there is no doubt that we occasionally meet with cases in which a slowly advancing fibrosis extends from the intermuscular septa into the muscle substance. The fibrous tissue produced is of great density and of very chronic formation. By its extension it leads to pronounced atrophy of the muscles which it involves, and at the same time leads to more or less complete fixation of the joints or parts in its neighbourhood. Such a fibrosis may affect the subscapular muscle, for example, and lead to complete fixation of the scapula to the thorax.

(2) **Inflammation (myositis).**—In considering the incidence of inflammation in muscles it is necessary to remember that we have to distinguish between the changes which concern the fibrous tissue which lies between the individual muscle bundles,

and the actual muscular elements themselves. In the case of the fibrous tissue we find a certain degree of separation of the fibrils by the œdema fluid that is poured out, together with a more or less marked accumulation of leucocytes within the meshwork. In the case of the muscular elements themselves neither of these factors is present, but we find that there is a loss of striation most marked of course in the case of the striated muscle, and a general hyaline appearance of the fibres. At the same time there is a loss of that definition of the outlines of the muscular bundles which is characteristic of the normal muscle.

Myositis is an invariable accompaniment of every inflammation that is taking place in the immediate neighbourhood of the muscle. Reference has already been made to this fact in connection with pericarditis and endocarditis, and it is generally true. In the same way if the inflammation in the neighbourhood is associated with the formation of pus the muscle itself becomes also involved. Thus in the case of an intense cellulitis of the arm the suppurative process penetrates between the layers of muscle along the intermuscular septa, and ultimately the muscles themselves may become broken down into pus.

Myositis ossificans.—This condition is one of extreme rarity and, so far as pathology is concerned, lies in a class intermediate between the inflammations and the degenerations. That is to say, it is probable that the disease commences in a myositis and that the inflammatory material becomes subsequently the seat of a calcification and ossification. The disease is a more or less general one, but there is a special tendency for the muscles of the back, and particularly for portions of the erector spinæ, to become affected. In the first instance the change commences in the intermuscular connective tissue, but as this proceeds to invade the muscle itself, the change comes to definitely involve the muscle, with the result that irregular particles of bone are formed in the very substance of the muscle. Hence, at first, the formation of bone takes place in immediate connection with the tendinous portions of the muscles, and in this point is to be seen a relation with such conditions as 'rider's bone,' &c. The change is an irregular, but a true, ossification.

(3) **New-growths.**—Primary new-growths of muscle are very rare if we except the formation of leiomyomata in the case of the uterus. In the voluntary muscles we occasionally meet with fibromata and lipomata, but these arise in the connective tissue of the muscle. Angeioma of muscle is excessively rare. There is, however, a remarkable specimen of the condition in the

Westminster Hospital Museum, in which the entire gracilis muscle is occupied by a cavernous angeioma, the blood spaces of which are, in many instances, as large as a small walnut.

Secondary invasion of the muscle by the various forms of malignant growth is, of course, common. Sometimes the invasion is marked by a fairly definite margin, but, as in carcinoma of the mamma, the great pectoral muscle may become invaded by the formation of a number of apparently disconnected nodules of new-growth. Such a mode of invasion is, however, rare, except in the instance mentioned.

Animal parasites.—The most important animal parasite which concerns muscle is the **Trichina spiralis**, the condition to which it gives rise being termed **trichiniasis**. The disease depends upon the ingestion of badly cooked pork which is infected with the parasite. On its arrival in the stomach the entozoa which were in the infected meat are set free and commence to develop. In a few days they produce ova from which the embryos are set free viviparously. These embryos at once commence to bore their way through the walls of the alimentary canal and penetrate into the muscles of the trunk, head and neck, and limbs. It is this process of invasion of the muscles of the host which is accompanied by the febrile and other grave constitutional symptoms of the disease.

When the embryos have penetrated well into the muscles, they coil themselves up and come to rest. Acting as irritants of a mild order in this resting stage, they lead to a moderate degree of inflammation around them, and ultimately to the formation of a capsule by the tissues of the host. This capsule is generally composed of fairly dense fibrous tissue, but sometimes it becomes calcified.

Certain other animal parasites have been described as occurring in muscles, but they are so rarely seen that their consideration need not detain us.

(3) TENDONS

In connection with the tendons it will only be necessary for us to mention two conditions, viz. tenosynovitis and ganglion. In other respects the tendons do not differ from other forms of dense fibrous tissue. Thus when they have been severed their ends undergo an inflammation and eventually become reunited by the formation of a fibrous tissue, they sometimes undergo calcification, and so on.

Tenosynovitis, in a certain number of cases, is really nothing more than inflammation which has extended from a joint to the sheaths of the tendons which pass over it. With this variety we are not concerned. But in other instances the condition appears to arise spontaneously. In them the inflammation is accompanied by great pain owing to the inextensibility of the parts affected, and at times the process may go on to suppuration. Such is the explanation of some cases of whitlow.

Special forms of tenosynovitis are found in connection with rheumatism and gout, and in the case of these diseases the inflammation of the sheaths of the tendons leads to the formation of adhesions and the consequent impairment of movement. At the same time the contraction of the adhesions leads to different varieties of deformity. One of the most characteristic of the deformities produced in this way is that known as 'Dupuytren's contraction.' It affects the fibrous tissue of the palm of the hand and the flexor tendons, and causes so great a contraction of the hand as to render the member useless.

A *ganglion* is, as a rule, a localised cystic dilatation of the sheath of a tendon. It is commonly situated either upon the dorsum of the hand or wrist, the dorsum of the foot, or more rarely in the palm of the hand. It may be only as large as a pea, or it may reach to the size of a pigeon's egg. Its wall consists of more or less delicate fibrous tissue which is fused on the outside with the fibrous tissue of the surrounding parts, and is lined within by an imperfect layer of endothelial cells. The contents of the cysts are sometimes quite fluid, but more commonly they are gelatinous in consistency, though colourless. As to the actual nature of the substance composing the cyst contents there is doubt. Some authors regard it as albuminous, others as gelatinous, and yet others as colloid or mucoid.

Another variety of ganglion is known which is termed the 'compound' or 'diffuse' to distinguish it from the 'simple,' of which the description has been given above. In this variety we frequently have to do with a dropsical effusion into the common sheath of a number of tendons (e.g. that of the flexors at the wrist). In other cases the pathology of the condition is uncertain, but since in them bodies are frequently found which bear a marked resemblance to certain of the 'loose bodies' of joints, it is not impossible that both conditions may have originated in the same way, viz. owing to a chronic inflammation. In fact, many forms of ganglion are probably tuberculous.

The free bodies which are found in compound ganglia are often termed 'melon-seed bodies' from their appearance. They are smooth colourless oval bodies of considerable hardness, which on section show a concentric arrangement. Microscopically, like certain varieties of the loose bodies of joints, they consist of a dense but imperfect kind of fibrous tissue, and are quite avascular.

(4) BURSÆ

Structurally, bursæ bear considerable resemblance to the sheaths of tendons. That is to say, their walls consist of a condensed layer of fibrous tissue lined on the inner side by a more or less perfect layer of endothelial cells similar to those of the pleura or peritoneum. Within the bursa is a serous or mucous fluid. Externally, the wall of the sac merges into the connective tissue of the part in which it is situated. Some bursæ, such as those under the deltoid muscle and over the patella, and many others, are constantly present, but new bursæ may be formed at any point which is exposed to unusual pressure. Such, for example, are the bursæ formed over the outer malleolus in tailors, over the ischial tuberosities in weavers, on the outer side of the head of the metatarsal bone of the great toe (bunion).

Nearly all the diseases of bursæ are inflammatory. The sole exception is hæmorrhage into the cavity of the bursa. Under these conditions the bursal cavity becomes filled with blood clot which undergoes the ordinary changes. It becomes decolourised, contracts somewhat, and, ultimately becoming organised, is converted into, or rather replaced by, fibrous tissue. If the clot becomes septic, it softens, breaks down into pus, and leads to the formation of an abscess.

Of the primarily inflammatory affections of bursæ, the most important are acute bursitis, chronic bursitis, and chronic thickening of the bursal walls.

Acute bursitis is generally the result of injury. The changes which accompany it are the ordinary changes of acute inflammation. Not infrequently the inflammation is sufficiently severe for pus to be formed. The acute pain of a bunion which is inflamed even short of suppuration is a matter of common experience; when suppuration occurs the inflammation may be so great that it extends well up the leg. Where the inflammation or suppuration affects a bursa of large size, such as those over the patella or over the trochanters, the constitutional disturbance is very severe.

Chronic bursitis is a condition in which there is an accumulation of fluid in a bursa owing to the occurrence of repeated small injuries which are not enough to lead to acute bursitis. The commonest form of this modification is 'housemaid's knee.' The wall of the bursa becomes somewhat thickened, and the fluid contents of the bursa become albuminous, and sometimes contain small flakes of fibrin.

Chronic enlargement of the bursæ is not very commonly found. In it the walls of the cavity become converted into a material of cartilaginous hardness whilst the cavity itself is reduced to small dimensions. The cause of the condition is repeated mechanical injury of a slight nature. In some cases of this kind in which the reduction of the size of the cavity is not so great, melon-seed bodies may be found similar to those which are sometimes found in ganglia. It is possible that the latter variety is sometimes tuberculous.

SECTION VII

THE PATHOLOGICAL ANATOMY AND HISTOLOGY OF THE VARIOUS PARTS OF THE DIGESTIVE TRACT

In order to save repetition and cross-reference, it will be advisable to consider the entire category of diseases of the mouth and naso-pharynx in this place, rather than to refer here only to those which have to do more particularly with the organs of digestion, and defer consideration of those which are especially associated with the respiration to another place.

(1) THE MOUTH AND NASO-PHARYNX

The morbid conditions of the mouth and naso-pharynx may be divided into the general and the special according as the process at work is liable to affect the entire tract or to be limited to one particular tissue.

A.—GENERAL DISEASES

Although the morbid conditions of the mouth and naso-pharynx manifest very different features in different cases, they all unite in being expressions of an inflammatory process. The inflammation may be acute or more or less chronic, it may be accompanied by a greater or less degree of destruction of the tissues of the parts, it may be associated with severe constitutional symptoms or not, but the pathological features of the conditions differ not at all in kind, but only in degree.

(1) The commonest affection of the tract is that which is summed up in the infective disease known as a **coryza**. In this disease the entire naso-pharynx becomes dry, red, and tender for a time, and subsequently red, swollen, and covered by a more or less tenacious mucous secretion. The condition has already been

described in some detail, so that it is not necessary to refer to it fully here. But it is important to note that the changes which are observed in the case of an ordinary 'cold' are almost precisely similar to those which constitute the earliest changes in an attack of whooping cough or one of acute exanthemata. In scarlatina, in measles, in variola, and to a greater or less degree in all the other exanthemata, there occurs an affection of the mouth and naso-pharynx. No doubt in scarlatina the pharyngeal mucous membrane, and particularly the soft palate and the tonsils, are affected more than other parts, while in measles there is a general catarrhal inflammation of the entire tract, and similar differences obtain in the case of the other exanthemata. But these facts do not vitiate the general truth of the statement.

(2) **Diphtheria.**—Although diphtheria is a disease which is not as a rule spread over the entire naso-pharynx at the same time in the same individual, it comes into the class under discussion owing to the fact that there is no part of the whole tract which may not show the presence of the characteristic membrane of the disease.

In diphtheria we have to do with an inflammation of such intensity that the tissues which are subjected to the action of the irritant undergo a necrosis in mass. Since these tissues are, at the time of their death, saturated with exudation fluid which coagulates in the meshwork of the tissue, the form of necrosis is that which is known as coagulative. The dead material is adherent to the underlying tissue and constitutes the diphtheritic membrane. Together with the disorganised elements of the mucous membrane, and the filaments of fibrin, microscopical examination shows that a moderate number of leucocytes, and varying numbers of diphtheria bacilli, are present. Sometimes there is a small admixture of red blood corpuscles, but this is never a marked feature of the membrane.

The commonest situation for diphtheria is the soft palate and the pillars of the fauces. The patches of membrane are then sometimes discrete and of small size, but sometimes the entire region is covered by a dirty grey membrane somewhat resembling wash-leather. The process may extend to the tonsils forming upon them patches of membrane or perhaps an entire covering. Starting in the faucial region, the disease may be more or less strictly localised there throughout, or it may extend either in the direction of the posterior nares or in that of the larynx. In either case the severity of the disease is much greater.

When a portion of diphtheritic membrane is caught with a pair of forceps, it is seen that it is more or less closely adherent to the tissue beneath, so that forcible removal is accompanied by slight bleeding of the raw surface left. When diphtheria travels to the nares or down to the larynx the membrane does not generally have the consistency that it has when present on the fauces. This is particularly noticeable when the nose is affected, and as a result one of the most characteristic symptoms of the extension of the process to this part is the occurrence of a sanguineous discharge from the nose. In the most severe cases of all, the disease affects the entire nasal mucous membrane and appearing at the anterior nares leads to excoriation of the skin surrounding the nostrils.

When the disease extends downwards from the fauces it may affect both the larynx and the œsophagus. In the latter situation it is, however, rare, as it is in the stomach; nevertheless, true diphtheritic membrane has been found in both of these situations. When the disease extends to the larynx—a very common occurrence—the symptoms to which it gives rise are those dependent upon the interference which it opposes to the entry and exit of air, both by its very presence and by the inflammatory swelling by which it is accompanied. Subsequently it is usual for a broncho-pneumonia to be set up.

Amongst the general diseases we have now to consider some which are general only in a restricted sense. Thus we meet with conditions in which the mouth is the sole seat of disease, others in which disease is confined to the pharynx, and again others in which the nose is affected. In all these cases, however, there is no hard and fast line of demarcation between the different portions of the tract.

(3) **Stomatitis.**—This condition is an inflammation of the entire mucous membrane of the mouth. It varies considerably in severity and depends upon a variety of causes.

(*a*) **Thrush.**—This, the commonest variety of stomatitis, is met with in infants who have become debilitated from bad feeding and in adults at the end of a long, exhausting, and fatal illness. It manifests itself by the presence of patches of a white material on the dorsum of the tongue, the insides of the cheeks, and the mucous membrane covering the gums. This white material consists largely of a mycelial growth which can be readily recognised under the microscope. The actual fungus which is present in thrush is a matter of uncertainty. It is generally said to be **Oïdium** or **Saccharomyces albicans**, but it is probable that under these names are included a large variety of different micro-organisms. The patch of fungus is not adherent to the tissues; beneath and around it is an area of congestion and slight inflammation.

(*b*) **Follicular stomatitis.**—A condition which is frequently confounded with thrush is simple follicular stomatitis. In it the mucous follicles of the buccal mucous membrane and the entire mouth become slightly inflamed and filled with their secretion. They therefore project somewhat above the general level of the mucous membrane. There is, however, no actual breach of surface, and although the hygienic factors which lead up to this condition are closely similar to those obtaining in thrush, there is not that association with a fungus in simple follicular stomatitis that is characteristic of thrush.

In some cases the simple follicular inflammation proceeds to a condition of definite ulceration. Under these circumstances numbers of small ulcers are visible over the mucous membrane. At the same time, owing to the severer nature of the condition, evidences of inflammation are visible on other parts than the follicles themselves. The bases of the ulcers are covered by a small greyish slough, and the intervening tissue is red and inflamed. Sometimes the ulcers coalesce, with the formation of large ragged sores. This is particularly liable to be the case when the ulcers are situated upon the gums, and then the alveoli of the teeth may become exposed.

(*c*) **Gangrenous stomatitis.**—This condition is also termed *noma*. It is the most formidable disease of the mouth. For it extends with great rapidity, and leads to a gangrene of considerable tracts of mucous membrane, and, being met with almost exclusively in children whose health has been undermined, it is nearly always followed by a rapid death. The actual amount of destruction that occurs in noma varies considerably; in one case there may be a small slough formed about the alveolus of one tooth, in another the entire cheek may be perforated. Slight cases such as those which have been mentioned are of very rare occurrence, for the conditions under which noma makes its appearance are such that when the disease has once manifested itself, it is very unlikely that it will become promptly arrested. Another name by which the disease is known is **cancrum oris**. This name is derived from a special manifestation of the disease. In cancrum oris one cheek, at the angle of the mouth as a rule, becomes red, swollen, brawny, and shiny. The entire thickness of the cheek is affected by an intensely acute inflammation which goes on to gangrene. Soon the redness passes into lividity, and then a central black spot appears which soon becomes the focus of a spreading gangrene. On the internal surface of the cheek there is a large ragged foul ulcer.

Gangrenous stomatitis is particularly a disease of very young children, but a similar condition may be met with in older patients as the result of ill-health and a carious condition of the teeth. In such a case the disease is especially manifested over the mucous membrane of the gums, and the entire lower jaw, for example, may be denuded owing to the removal of its mucous membrane, and the separation of its periosteum by extension of the disease. Here, of course, the stomatitis is associated with necrosis of a portion or the whole of the bone.

Stomatitis of a very severe kind may be, as in the instances which have been just given, set up by the action of micro-organisms. As to the actual nature of these micro-organisms we are in doubt, and it is possible that the same varieties are not to be inculpated in all cases. The extensive flora of the mouth renders an examination into this question one of extreme difficulty. It may be said, however, that we are particularly likely to find streptococci in such cases. Some authors have ascribed the condition to the action of diphtheria or diphtheria-like bacilli.

In certain instances we meet with severe forms of stomatitis as the result of the absorption of chemical poisons. Thus mercury is always liable to produce salivation and looseness of the teeth when given in doses beyond the physiological limit. That limit varies considerably in different individuals, but in all a point can be reached at which a stomatitis commences to appear. The same is true of arsenic and of phosphorus. In the case of phosphorus, indeed, the stomatitis is of so severe a kind that it is accompanied by a more or less severe necrosis of the bone of the lower jaw.

These agents act in different ways. In the case of mercury and arsenic, it is probable that the poison is in part excreted by the saliva, and therefore has especial chances of attacking the mouth. In the case of phosphorus, it is the fumes which produce the mischief, and they appear to attack the jaw first at the situation of a carious tooth. This form of necrosis of bone is met with almost exclusively in persons engaged in the manufacture of those matches for which ordinary, and not amorphous, phosphorus is used.

(4) **Granular pharyngitis.**—In the case of the pharynx we meet with several morbid conditions that may be spoken of as general, though in a more restricted sense than those diseases of

the mouth which are summed up under the name 'stomatitis.' Thus there is a more or less chronic condition which affects the entire pharyngeal mucous membrane, and is termed **granular pharyngitis**. In it the principal features are the redness of the mucous membrane, and the presence on it of a number of small bright red projections, each about as large as a pin's head. These projections are minute varicose veins, and the whole change is one of a chronic inflammation with congestion. The irritant is not always the same. In one case it may be excessive smoking, in another it may be an expression of an undue indulgence in alcohol, and in yet a third it may depend upon exposure to cold and severe straining of the voice.

(5) **Adenoids.**—A very common condition, especially in young children, is that in which there is a general hypertrophy of the lymphoid tissue in the pharynx. At the upper part of the pharynx attached to the base of the skull is a mass of lymphoid tissue which is frequently called the pharyngeal tonsil. In certain children this mass of lymphoid tissue undergoes considerable hypertrophy, and forms a number of polypoid growths which protrude into the pharynx and ultimately come to block up completely the posterior nares. The change is special to the pharynx in the sense that it is especially this mass of lymphoid tissue which is liable to undergo hypertrophy, but it is general in that the tonsils and all the lymphoid tissue of the mouth join in the overgrowth. Indeed, one might go further, and say that in these cases there is a general tendency for an overgrowth of the lymphoid tissue throughout the body. The hypertrophied tissue maintains its normal histological composition so far as concerns the fact that it consists of a fibrous-tissue meshwork holding vast numbers of lymphocytes, but it differs from normal lymphoid tissue in the fact that there is present a larger amount of fibrous tissue than normal. This gives to the mass a greater density than normal, a feature which is equally well shown by tonsils that have undergone chronic hypertrophy.

The presence of post-pharyngeal adenoids leads to changes in the pharyngeal mucous membrane. It becomes the seat of a chronic catarrhal inflammation. This inflammation extends to the neighbouring parts, particularly the nares and the Eustachian tubes. As a result a chronic rhinitis, with thickening of the nasal mucous membrane, is set up, on the one hand, and on the other, the chronic inflammation extends up to the middle ear, and often produces permanent and serious damage. Temporarily, post-pharyngeal adenoids of any size always produce deafness, owing to the closure of the Eustachian tubes by the swollen and inflamed mucous membrane.

(6) **Pharyngeal abscess.**—An important, but not a very common, morbid condition of the pharynx is abscess. The condition is almost always due to disease of some of the cervical vertebræ, and the resulting abscess may be so large that it interferes considerably with deglutition and respiration.

In the case of the nose the general conditions are diphtheria, coryza and allied diseases, to both of which we have already referred, certain of the chronic infective inflammations, chronic rhinitis, ozæna, and mucous polypi. Several of these conditions, too, might equally well be regarded as belonging to the special, as distinguished from the general, class.

(7) **Chronic rhinitis.**—In chronic rhinitis we have a general thickening of the mucous membrane of the part. This is accompanied by a chronic catarrh, a proliferation of the investing cells of the mucous membrane, and frequently by a loss of much of the ciliated epithelium. By some authors the condition is held to be associated with the presence of the diphtheria bacillus. As its name implies, the condition is one of great chronicity.

(8) **Chronic specific inflammations of the nose.**—The members of the group of chronic inflammations which are particularly liable to affect the nose are glanders, syphilis, tuberculosis, and rhinoscleroma. Leprosy and lupus also occur, but are less common. In the cases of glanders and rhinoscleroma the mucous membrane is particularly affected, and the diseases in question may be said to have an especial proclivity for the nose. In the case of the other diseases mentioned, although the nasal changes produced may be most severe, it cannot be said that they are more than particular examples of changes which are liable to be produced anywhere.

In the case of all the diseases of the chronic inflammatory group, the characteristic lesion is a nodule of inflammatory material, whether composed of cells alone or composed of granulation tissue. Nodules of this kind form on the mucous membrane of the nose, break down on the surface, and give rise to small ulcers with sloughy bases from which a sanguineo-purulent discharge escapes. In the case of rhinoscleroma, a disease which is but rarely seen in this country, the inflammation leads to a general thickening of the mucous membrane of the nose, and often spreads thence to the pharynx and larynx. Superficial ulceration may occur, but extensive destruction of tissue such as occurs in syphilis, for example, is seldom met with.

Syphilis and tuberculosis of the nose are of especial importance in connection with the production of two varieties of the condition known as **ozæna**. In ozæna the characteristic symptom is the existence of a singularly foul smell which is always perceptible at a little distance from the patient and may be perceptible by the patient himself. It depends upon the ulceration that is going on in the nose.

In tuberculosis the condition may or may not be associated with destruction of bone, but in the case of syphilis such caries is constant. Not all ozæna depends upon either tuberculosis or syphilis, however; the condition will arise under all circumstances in which a putrescible material is confined in the nose and there undergoes putrefaction. It may therefore occur in ordinary chronic rhinitis, or in any of the other chronic inflammations that have been mentioned. Nevertheless, it is most commonly associated with disease of bone, and therefore with tuberculosis and syphilis.

Syphilis has been mentioned as a cause of general disease of the mouth and naso-pharynx. As a matter of fact, it is far more important than would have appeared. For, as has been said when considering syphilis as an infective inflammation, some of the most marked changes which occur in the course of the disease are those which constitute the secondary and early tertiary manifestations, and which are particularly liable to concern the mouth, fauces, pharynx, epiglottis, and larynx. Thus we may meet with a case in which mucous tubercles are present over a large portion of the buccal mucous membrane, while ulceration is taking place in the soft, and perhaps in the hard, palate, in the epiglottis, and in the larynx. With regard to the nose in syphilis, we have to distinguish two varieties of affection. The one is certainly tertiary, and it is this which is so frequently associated with destruction of bone and ozæna; the other is that affection which constitutes 'snuffles' in children the subjects of congenital syphilis. In the latter instance there is much reason for considering that the condition is not tertiary, but rather secondary, in a large number of cases. In addition to this general affection of the mouth and naso-pharynx by the syphilitic lesion, as will be seen later, we have also to recognise that the disease has tendencies to affect special parts, leading in them to the appearance of somewhat characteristic changes.

(9) **Nasal polypi.**—These growths are far more commonly met with in young adults than in any other class of patient. As a rule, they are about the size of the end of the finger and possess

a broad basis of attachment. They are pale in colour, and may usually be recognised easily by examination of the anterior nares. They consist histologically of elements similar to those of the mucous membrane of the nose, and it is quite justifiable to speak of them as localised hypertrophies of the mucous membrane. At the same time they are not absolutely similar in composition, for the fibrous tissue lying beneath the epithelial covering is loose and œdematous, and often shows a considerable degree of mucoid degeneration. The epithelial covering consists of columnar cells which are sometimes ciliated. The growths are generally attached to the superior or the middle turbinated bone. They are very frequently associated with the presence of post-pharyngeal adenoids. Besides the actual interference that they present to respiration through the nose, polypi induce, and keep up, an unhealthy condition of the nasal mucous membrane. They are therefore liable to be accompanied by chronic nasal catarrh, and this, if it be prolonged, leads to an alteration of the mucous membrane of a permanent kind and a permanent impairment of the sense of smell. They are not infrequently associated also with chronic enlargement of the tonsils.

B.—MORBID CONDITIONS OF SPECIAL PARTS OF THE MOUTH AND NASO-PHARYNX

(1) **The lips.**—The lips are liable to be affected by any of the changes occurring in their neighbourhood, whether on the outer surface of the face (as in lupus), or within the mouth (as in stomatitis). But with these we are not now concerned. The special conditions that we have to consider are carcinoma and macrocheilia.

(*a*) **Carcinoma.**—Carcinoma of the lip is of very common occurrence. It manifests itself by the presence of a small elevated mass which undergoes a slight amount of superficial ulceration, particularly on the mucous surface. The base of the growth is extremely hard, and the entire growth may be taken between the fingers and then appears to be somewhat strictly localised, and recalls in feeling a hard chancre. This point is one of importance, since a hard chancre is occasionally seen in this situation. The mass of carcinoma is far more commonly met with on the lower lip than elsewhere. Frequently it occurs at a point which has been chronically irritated by a pipe in smoking, a fact that has been adduced in favour of the view that carcinoma is induced by mechanical irritation.

Histologically the growth is a squamous-cell carcinoma. The downgrowth of the epithelium in the neighbourhood of the mass is usually well marked, and the number of cell-nests is generally great. The disease, if unremoved, extends with sureness, but not commonly with great rapidity, so far as the local condition is concerned. But the submaxillary glands become secondarily affected fairly early in the disease, and the death of the patient is brought about by the extension of the growth in these glands, their ulceration, and the exhaustion, and perhaps hæmorrhage, which that ulceration produces.

(*b*) **Macrocheilia.**—In this rare condition the tissues composing the lip or lips undergo a great increase in growth. The fundamental change consists in a dilatation of the lymphatics of the part, with the formation of a condition of lymphangeioma. The increase in the amount of lymph in the tissues is accompanied by their overgrowth, so that the ultimate result is somewhat similar to that which constitutes elephantiasis in the limbs. The principal difference between macrocheilia and elephantiasis, however, lies in the fact that while elephantiasis is an acquired disease, macrocheilia is in most cases congenital or depends upon a congenital defect. On section a macrocheilia shows that it consists of a number of greatly dilated lymph spaces which are separated from one another by a well-formed fibrous tissue. The layers of the epidermis and epithelium are more numerous than normal.

(2) **The tongue.**—The tongue is liable to a large number of pathological alterations. It is altered in appearance in acute febrile conditions, it may be the seat of inflammation, it may undergo atrophy, and it may be the seat of a new-growth.

(*a*) **Fever.**—It is one of the best recognised facts that when a patient is febrile his tongue manifests an alteration of its coat. This alteration essentially consists in a difference in the degree to which it is covered by epithelium. At the commencement of a febrile attack, or during the whole course of an attack which is only accompanied by a slight rise of temperature, the dorsum of the tongue is whiter than normal over its whole surface. The white coat is thin, and it is possible to see, on careful examination, the summits of the filiform papillæ. This constitutes the *stippled* tongue. If the fever becomes more acute, the amount of white coat increases until it covers in the tips of the papillæ, and then there is a uniform white, smooth, and shiny appearance of the dorsum. This is the *plastered* tongue, and it may always be taken as an indication that the patient is in an acutely febrile condition. Sometimes the tips of the papillæ become again visible, owing to the removal of a portion of the coat forming the plastered tongue. They are then of a bright red colour, and show very plainly against the dead white of the coating which lies between them. Such a tongue is termed a *strawberry* tongue, and it undoubtedly bears a great resemblance to a white strawberry. If the fever continues the white coat becomes brown along the centre, and portions of it become separated and cast off. Such a tongue is said to be *bare* or *denuded*, and is a sign of grave import. The patient in whom such a tongue is found is always dangerously ill. A further stage of denudation is that in which the entire dorsum of the organ becomes bare, red, and cracked.

In all the conditions which have been mentioned above the tongue is deficient in moisture. With the stippled tongue the deficiency is not great, but with the red denuded tongue the normal moistness of the mouth may be replaced by the presence of a small amount of extremely viscid secretion alone. The amount of moistness therefore has an important significance. For when a tongue which was at one time dry becomes again moist, we know that the patient is on the mend. This improvement is accompanied by an alteration in the appearance of the tongue. For the coat begins to disappear. But, instead of disappearing along the middle of the dorsum, as it does in the formation of the denuded tongue, it disappears first at the tip and along the edges. Such a tongue is termed a *cleaning* tongue, and the removal of that portion of the coat or fur which lies far back and in the middle line is the last sign of convalescence.

Histologically the changes are all dependent upon the length of the papillæ and the amount of epithelium which covers them and lies between them. In the denuded tongue the papillæ are quite bare, being covered by a much thinner layer of epithelial scales than in health. In the plastered tongue, on the contrary, the layer of epithelial cells, both desquamated and adherent, is double or treble the thickness present normally. At the same time the layers of epithelium become dry and hard, owing to the deficiency of buccal secretion and the increased rate of respiration by which the fever is accompanied.

(*b*) **Variations in size.**—The tongue being a muscular organ is liable to a true muscular atrophy. As a rule, this change is limited to one half of the tongue. The change depends upon some cause which interferes with the conductivity of the fibres in the hypoglossal nerve, whether that cause acts upon the centre in the bulb or on the nerve itself in some part of its course. The muscle of the affected half may show some fatty degeneration; but as a rule it offers no alterations in its appearance beyond its diminished size and a general lack of tone. So far as the nerves themselves are concerned the one supplying the atrophied half of the tongue almost always shows a definite sclerosis of its fibres. The specimens from which figs. 168 and 169 were taken are of this kind.

A condition analogous with macrocheilia is sometimes seen to affect the tongue. It leads to the condition known as **macroglossia.** In macroglossia the tongue may be so considerably enlarged that it is impossible for the mouth to be closed. The tongue then becomes hard and dry on the surface, and the patient's condition is a pitiable one. The change depends upon a lymphangeiomatous condition of the lymphatics of the part.

(*c*) **Inflammation (glossitis).**—Acute inflammation of the tongue is of rare occurrence; it is generally seen as a part of a general acute stomatitis. When it occurs the tongue is enlarged and acutely tender and painful. That it is in some degree œdematous is shown by the fact that impressions of the teeth are visible on its edges.

Small ulcers are sometimes seen on the sides of the tongue; they result from the irritation of carious teeth, and have no particular histological characters. They are of importance, however, in that they may become the seat of a carcinomatous growth if the irritation continues.

Chronic inflammation of the tongue is almost always syphilitic. It shows itself under two forms. In the one the epithelium of the tongue is greatly thinned and so smooth as to be shiny. In the other the organ is covered by a number of smooth opaque white plates, the disposition of which recalls the appearance of the scales on the back of a crocodile. This condition is also known as **leucoplakia.** A condition resembling leucoplakia is also met with in persons who are great smokers. How far the condition can be caused by smoking alone, apart from syphilis, is a matter of doubt.

Syphilis also occurs in the tongue in the form of gumma. The gummatous mass is then formed in the actual substance of the organ, and, undergoing the liquefaction and breaking down which are characteristic of gummata, gives place to the formation of a ragged ulcer with foul sloughy base. It is then easily mistaken for a carcinomatous ulcer.

Tuberculosis of the tongue is somewhat rare. It usually manifests itself by the presence of small ulcers on the dorsum and sides of the organ. Rarely one meets with ulcers of larger size, and these are very likely to be mistaken for carcinoma, the diagnosis only being made when sections are examined microscopically. Tuberculosis of the tongue is generally found in association with tuberculosis of the lungs. But it must not be supposed that every ulcer of the tongue met with in a patient, even in an advanced condition of pulmonary tuberculosis, is itself tuberculous. For in the debilitated condition which accompanies the latter stages of tuberculosis, ulcers are liable to be formed on the tongue, as elsewhere, which are quite simple.

(*d*) **New-growths.**—By far the commonest form of new-growth in the tongue is carcinoma. Fibromata, lipomata, and certain other forms of tumour have been described, but they are so rare that they may be ignored here.

Carcinoma of the tongue is of the squamous-cell variety. It may commence either at the side of the organ, or on the dorsum, or in the floor of the mouth about the frænum. As a rule, the growth commences somewhat far back, and if it commences on one side of the organ, it shows little tendency to pass beyond the middle line. On the other hand, carcinoma of the tongue is one of the most rapidly growing forms of carcinoma, in this respect affording an exception to the general law that the squamous-cell carcinomata are the least rapidly growing carcinomata. The tumour first shows itself as a small papule or ulcer, which rapidly grows and provides itself with a hard base. It usually extends in the direction of the floor of the mouth, and very soon after its commencement secondary enlargement of the lymphatic glands beneath the jaw supervenes. The histological characters of the growth present nothing uncommon. Cell nests may be few or many.

(3) **The teeth and gums.**—It is impossible to enter into a full description of the various morbid conditions that affect the teeth. We shall only mention those which come within the bounds of the general as distinguished from the dental pathologist.

Caries of the teeth is a process which is different from caries of bone in more than those points that depend upon the extreme hardness of the enamel and dentine. The process is a slow one and works from without. The first cause of the change consists in a small lesion of the enamel, by way of which some of the bacteria inhabiting the mouth find access to the dentine and ultimately to the pulp of the tooth. In their growth there they are aided by the putrefaction of particles of food which become lodged in the crevices of the teeth when sufficient care is not taken in their cleansing. Hence the process is a more definitely chemical and bacterial one than it is in the case of bone, where it is largely phagocytic. Nor do osteoclasts play the same part. In caries of the teeth they do not enter into the question until very late. Caries of the teeth themselves is not generally associated with caries of the bone of the jaw. Yet it may be so in cases in which the dental process largely involves the fangs. For then the carious fang serves as an irritant to the periosteum of the jaw, and leads to an inflammation which is always accompanied by pus formation. This periostitis is of slight amount if the tooth be removed, but if it be suffered to remain *in situ*, the periostitis extends and leads to a more or less extensive necrosis of the jaw.

A fairly common condition in connection with the roots of the teeth is the formation of a new-growth in the gum. Such new-growths commence in the bone of the jaw, or in the periosteum, close to the root of the tooth, and, increasing in size, come to form a definite tumour on the alveolar surface. The condition is known as **epulis.** In some instances the growth is a simple fibroma, in others a typical myeloid sarcoma. Epulis tends to increase locally, though somewhat slowly, but it has no tendency to form secondary growths.

In connection with the teeth one occasionally finds cysts and new-growths in the jaws which are dependent upon errors in development. These are known as **dental cysts** and **odontomata** respectively. Dental cysts may be unilocular or multilocular. The unilocular cysts have their origin in teeth that have not undergone eruption, and a tooth or pieces of dentine are usually found in their walls. Multilocular cysts appear to have developed out of a gland-like substance which has undergone colloid degeneration. They therefore have close analogies with the adenomata, and in some cases masses of epithelial cells are present. It is commonly held that these cysts depend upon a prolongation downwards of the epithelium of the jaw similar to that which normally occurs in the embryo to form the enamel organ. These cysts are generally non-malignant, but sometimes they approach, in histological arrangement and in tendencies, somewhat closely to the carcinomata.

Odontomata are rare tumours which consist of dentine and enamel and arise in connection with teeth retained within the jaws by faulty development. They are usually of small size, but one is preserved in the Museum of St. George's Hospital which is as large as a walnut. Exostoses or osteomata are of more frequent occurrence. The tumours are not really composed of bone, but rather depend upon inflammatory changes in the cement.

Before passing from the consideration of the teeth mention must be made of the changes which occur in the central upper incisors of the permanent set as the result of congenital syphilis. These teeth are narrowed towards the cutting edges so that they have the shape of a peg-top. In addition it is very common for the cutting edge to manifest a crescentic notch. The changes are probably due to a syphilitic inflammation of the jaw during the period of dentition, and are very often associated with interstitial inflammation of the cornea. It is necessary to remark that the only teeth in which changes of the kind mentioned are of diagnostic importance are, as has been said, the two central upper incisors of the permanent set.

(4) **The antrum.**—Though this cavity is not often diseased, it is liable to be affected by inflammation and by certain forms of new-growth. In inflammatory conditions the antral cavity may become filled with exudation fluid which is largely mixed with mucus, or with pus. In either case occlusion of the outlet causes the condition to be associated with very definite symptoms. The new-growths of the antrum are either sarcoma or a somewhat peculiar kind of growth which has many resemblances to the carcinomata. In the case of sarcoma the tumour may be myeloid, or may be composed of round or spindle cells; it is in the latter an intensely malignant growth. In that form of growth which resembles carcinoma the histological characters are almost exactly similar to those of a columnar-cell carcinoma, except that the alveoli are more regular and even in size. That the growth is not a carcinoma, however, is shown by the fact that it is non-malignant. It appears to result from a degeneration of an adenoma, the central cells of the alveolar masses undergoing a colloid or mucoid change. The condition is a very rare one.

(5) **The tonsils.**—Three conditions require notice in connection with the tonsils, viz. hyperplasia, inflammation, and the formation of new-growths.

(*a*) **Hyperplasia** is a condition which is very common in children in association with a general increase of the lymphoid tissue throughout the body. It is especially liable to be found in those who live under unsanitary conditions, and frequently exists in combination with adenoids and nasal polypi. Reference has already been made to the latter conditions, and it has been stated that they are a common cause of a general catarrhal inflammation of the naso-pharynx and of deafness. The tonsils themselves are not only enlarged so that they project, and may almost meet across the fauces, but are much firmer than normal. This change is due to the presence in them of an inordinately large amount of fibrous tissue. The follicles which lie on their surfaces are proportionately deep in these cases, and often are blocked with secretion.

(*b*) **Inflammation** of the tonsils (**tonsillitis** or **amygdalitis**) is of common occurrence. It forms part of the early stages of most of the acute infective fevers—in fact, it is probable that the tonsils are in many instances the site at which the infection gains its first entrance into the body. But the tonsils may be affected with an inflammation which is not part of a general infective condition in the sense in which that term is generally used. Thus we meet with a tonsillitis which is quite local and is apparently closely associated with exposure to cold, or to bad smells.

In tonsillitis the tonsils are red and inflamed, swollen, and tender, so that swallowing becomes exceedingly painful. The inflammation is not entirely confined to the tonsils themselves, but extends for a greater or less extent over the mucous membrane in the neighbourhood. On the surface of the tonsils the catarrhal nature of the inflammation is generally indicated by the presence of a number of yellow points. These points are situated over the mouths of the mucous crypts of the tonsil and depend upon the fact that the formation of mucus in them has been so voluminous that it has not been able to escape entirely. Not infrequently the accumulated secretion is present in masses so large that the entire tonsil becomes covered with a viscid yellow continuous layer of secretion. Under these circumstances the appearance is very similar to that of a membrane on the tonsil, and the condition may be mistaken for diphtheria. This mistake is the more easily made in that the secretion adheres somewhat closely to the surface of the tonsil, owing to the prolongation of processes of the secretion from the under surface of the mass into the crypts themselves. When removed, however, the mass of secretion does not leave a raw and bleeding surface beneath as in the case of diphtheria.

A tonsillitis of this description may recede after a time, or it may go on to suppuration with the formation of an abscess of the tonsil. This condition is known as **quinsy**. Its occurrence is accompanied by a marked aggravation of the pain and constitutional symptoms and by the formation of a fluctuating swelling in the affected tonsil.

(*c*) **New-growths** of the tonsil are very rare, even when they involve it by extension from parts in the neighbourhood. Primary carcinoma of the tonsil is, however, known, and is almost always of the squamous-cell type. In this connection it is important to remember that cell nests resembling in all respects those which are met with in squamous-cell carcinoma, are occasionally met with in the normal tonsil. Failure to remember this fact may lead to a mistaken diagnosis. Owing to the softness of the tissues, carcinoma in this situation progresses with great rapidity.

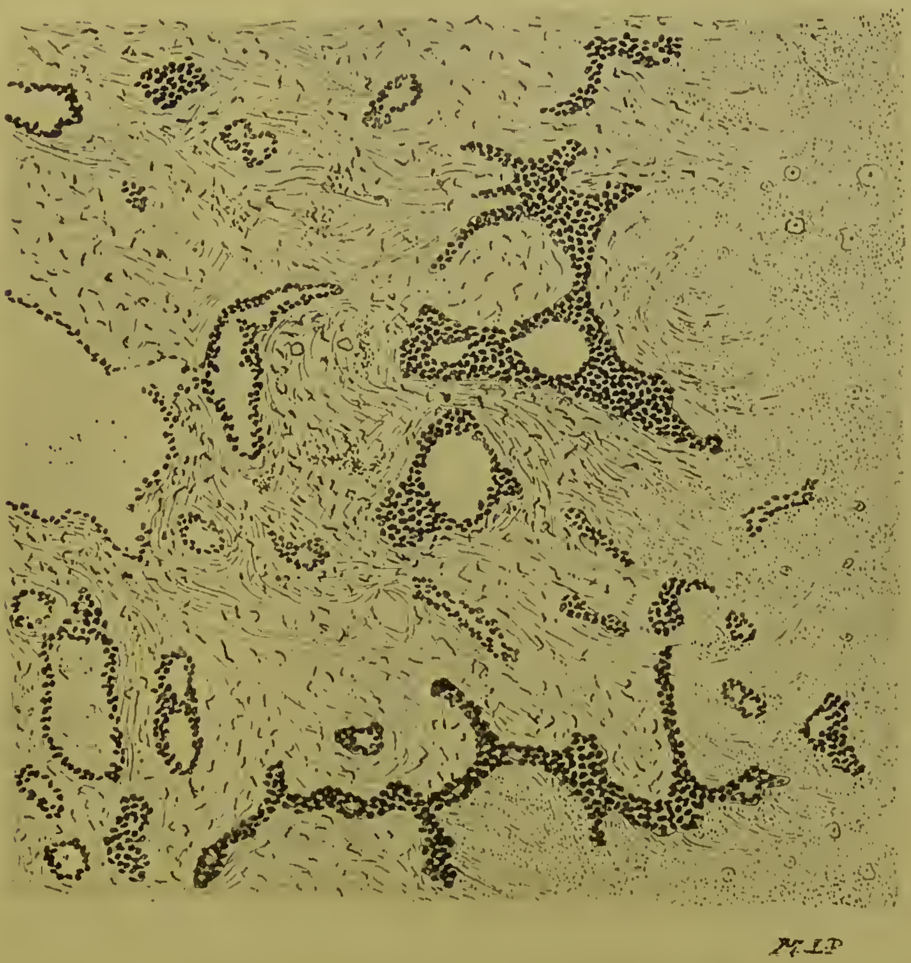


FIG. 91.—SECTION OF PAROTID TUMOUR. × 420.

To the right is a mass of hyaline cartilage, with a few cartilage cells present in it. This passes gradually into tissue having the characteristics of fibro-sarcoma of the hard type, but carrying irregular clefts and spaces lined by epithelium similar to those of fibro-adenoma. On the left is a clear homogeneous space of myxomatous tissue.

Rarely the crypts of the tonsils are the seat of **calculi**. These calculi are found generally in the case of tonsils that have long been the seat of a chronic inflammatory hyperplasia. They are of no special significance, excepting that they are apt to lead to suppuration. Their composition is very uncertain and inconstant, but calcium salts almost always are present in relatively considerable amount. They are always of small size, rarely exceeding that of a hemp seed.

(6) **The salivary glands.**—The salivary glands are not very liable to disease, but the affections which attack them lead to very characteristic conditions.

(*a*) **Inflammation** of the salivary glands is met with as a highly characteristic feature of the infective disease of **mumps**. In this disease the salivary glands, parotid and submaxillary, become enlarged and extremely painful. Sometimes the inflammation in the parotid ends in abscess, but this is very rare. The disease is not one which affects the salivary glands alone, although its commonest and most characteristic situation is in them. In severe cases it also leads to swelling and inflammation of the testicle. Contrariwise, acute orchitis may be associated with pain and swelling of the parotid gland.

(*b*) **New-growths** of the salivary glands are almost completely confined to the formation of those composite varieties of tumour which are generally spoken of as 'parotid tumours.' The growths in these cases are, in reality, fibro-myxo-chondro-adeno-sarcomata, but the sarcomatous character of the growth is so little in clinical evidence that the tumours are practically non-malignant. The growths probably arise owing to some slight error in development, and the presence in them of cartilage is taken to show that they have, in part, originated in an included portion of a branchial arch. In rare instances these growths may become definitely sarcomatous.

(*c*) **Cysts** in the floor of the mouth are not of very uncommon occurrence, as the result of the blocking of the duct of the submaxillary gland by a salivary calculus. Such cysts are termed **ranulæ**. They form tense swellings which give exit on puncture to a thin watery fluid. The salivary calculi themselves are usually composed of calcium phosphate, and not only may be found in the submaxillary, but also in any of the other salivary glands. As a rule they lie in the duct, but sometimes they are found in the substance of the gland itself. Ranulæ may terminate in the formation of an abscess or a fistula, if the cause of the obstruction is not recognised and removed in time.

SECTION VIII

THE DIGESTIVE TRACT—continued

(2) THE ŒSOPHAGUS AND STOMACH

We now pass to the consideration of those parts which are not common to alimentation and respiration, but are concerned with alimentation alone. Although the various morbid conditions which we shall have to notice in many instances are not confined to one anatomical portion of the alimentary tract, it will be convenient to keep to the ordinary anatomical divisions of the tract for purposes of description.

A.—THE ŒSOPHAGUS

By far the most important of the diseases of the œsophagus is carcinoma, not only in respect of the severity of the disease itself, but also in respect of the fact that it is one of the commonest situations in which carcinoma is found.

Carcinoma of the œsophagus is generally met with in one of three situations. It may be present at the commencement of the tube where it joins the pharynx, it may be met with in the middle, at a point corresponding to a little above the bifurcation of the trachea, or it may be met with at the cardiac end of the tube. Of these three situations the two former are commoner than the third. Nevertheless, the lower end of the œsophagus often becomes involved by extension upwards of carcinoma of the cardiac end of the stomach.

The actual growth itself may be accompanied by much or by little ulceration. Where there is much ulceration there is generally little anatomical stenosis, and where ulceration is slight the stenosis may be sufficient to prevent the passage of more than a fair-sized catheter. In this respect it is important to note that the amount of anatomical stenosis is no infallible measure of the amount of functional stenosis. Cases are frequently met with in which all the stenotic symptoms of the disease have been clinically present, and in which, nevertheless, at the autopsy, the disease has been found to have led to so great an ulceration that at the principal seat the diameter of the œsophagus is doubled or trebled.

The disease generally shows a tendency to surround the tube, and to extend for a certain distance in its length. In some cases this extension is small, the entire ring of carcinoma being less than an inch in any direction. In other cases, and these are generally associated with much ulceration, the disease extends along the œsophagus for a distance of five or six inches. The degree to which the disease extends to neighbouring parts varies considerably in different cases. In one there may be little more than a general thickening of the tissues lying between the œsophagus and trachea, in another the growth may have extended widely, and may finally perforate into the trachea or one of the bronchi. At the same time the degree to which the lymphatic glands are secondarily involved differs somewhat, though not to so great an extent as it does in the case of the primary growth. In most instances the cervical and bronchial glands are markedly infiltrated with growth.

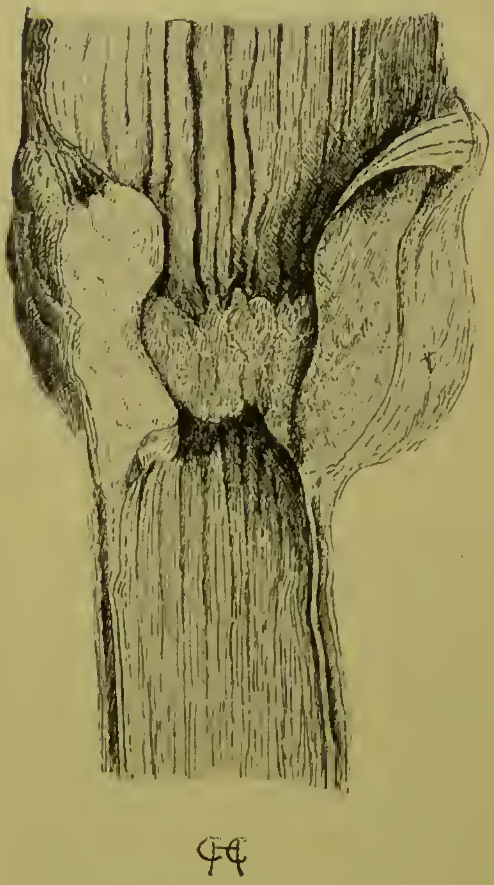


Fig. 92.—Malignant Disease of Œsophagus. $\times \frac{5}{6}$.

A ring of squamous-cell carcinoma has encircled the œsophagus and led to great stenosis. It occurred at the level of the cricoid cartilage.

The variety of carcinoma present in the œsophagus is, as might be expected, in most cases of the squamous-cell type. Occasionally, however, we meet with spheroidal-cell carcinomata. This is particularly the case when the disease affects the cardiac orifice of the tube, and then it is a question whether we have not to do with a true carcinoma of the cardiac end of the stomach rather than one of the œsophagus itself. But sometimes this possible escape from a difficulty is denied us. For we may meet with spheroidal-cell carcinomata affecting the upper or middle third of the œsophagus.

Sometimes nodules of carcinoma are formed at a small distance from the main growth along the length of the tube. These discrete nodules generally lie immediately beneath the mucous membrane, and do not show any tendency to ulcerate. They must not be confused with the small localised thickenings of the mucous membrane which are liable to be found in any case in which the tube is the seat of a chronic irritation, and which are therefore frequently seen in cases of œsophageal carcinoma. These thickenings are definitely situated in the epithelial covering and are akin to the corns found on the heart. They simply consist of heaped-up epidermal scales.

Sarcoma affects the œsophagus in rare instances. It usually forms a soft growth of considerable size which is apt to encircle the tube and to undergo great superficial ulceration. The condition is usually regarded as being carcinomatous until the microscope reveals the mistake. Small leiomyomata, fibromata, and lipomata have been found in the wall of the œsophagus, but are excessively rare.

Stenosis of the œsophagus is not always due to the presence of a carcinomatous stricture. It may depend upon the formation of a cicatrix in the tube after a traumatic injury. The most important of these are injuries produced by swallowing corrosive poisons, such as the strong acids and alkalies. In those cases in which the patient survives, the formation of a cicatrix necessarily follows, and as this contracts a stenosis is produced which does not differ in its mechanical effects from a stricture due to any other cause.

In the case of stricture of the œsophagus, as in the case of any other muscular tube, the part above the constriction becomes dilated and hypertrophied. The degrees of hypertrophy and dilatation differ in different cases. They are apt to be greatest when the stricture is one following on traumatism. In such cases a veritable **pouch** may be formed above the constriction. In other cases pouches and diverticula in the œsophagus depend upon traction from without the tube. Thus they may occur in conjunction with calcareous bronchial glands resulting from tuberculosis, or masses of fibrous tissue resulting from some inflammatory process, such as syphilis, in the same region. Under these circumstances the diverticula are generally small, and may be multiple.

A special variety of dilatation and hypertrophy is that which depends upon no known cause, and is therefore termed **idiopathic.** The dilatation and hypertrophy in such cases are considerable. The œsophagus may become converted into a fusiform sac with a diameter of as much as three inches at its greatest point. At the same time the length of the tube is generally increased, so that the œsophagus of a child of nine years may be even longer than that of an adult, and the muscular wall is perhaps three-eighths of an inch in thickness. The condition is a rare one, nor is it generally recognised during life; its ætiology is unknown, but there can be little doubt that it must depend upon an obstruction lower down which, since no anatomical evidence of it can be found, we are accustomed to consider may be a functional muscular spasm.

A morbid condition of the œsophagus of great importance consists in the existence of a **varicose condition of the veins** around its lower extremity. This change is generally found in cases in which there is an obstruction to the passage of the blood through the portal canals, as, for example, in chronic fibrosis of the liver (cirrhosis). The œsophageal veins form one of the means of communication between the systemic and the portal venous systems, and when the flow through the liver is impeded these anastomotic branches become dilated and tortuous. They may then be seen as a purple ring around the lower end of the œsophagus which extends for about an inch up the tube. The actual veins are sometimes to be seen projecting into the lumen of the œsophagus. The importance of the condition lies in the fact that these veins are liable to rupture and give rise to considerable hæmorrhage.

B.—THE STOMACH.

Owing to its large size and to the situation which it occupies in the function of nutrition, the stomach is liable to a very large number of morbid processes. Many of these—e.g. a large number of those which are concerned in the production of the conditions summed up under the name of ‘indigestion’—are associated with very slight anatomical changes, or even with no known anatomical changes at all. On the other hand, we meet with conditions in which the wall of the stomach is profoundly altered, and in these instances the digestive function has generally been no less profoundly modified, although cases are not of very infrequent occurrence in which at the autopsy disease of the stomach is found of which there was not the least suspicion during life.

(1) **Inflammation (gastritis).**—Our knowledge of the changes accompanying gastritis is extremely meagre. It is principally derived from cases in which a gastric fistula has become established owing to some injury.

(*a*) In **acute gastritis** the mucous membrane of the stomach becomes red and congested. Numerous small elevated red points are visible over its whole surface, but there is no secretion of gastric juice. On the other hand there is a greater formation than normal of mucus. Sometimes small erosions of the mucous membrane are formed, and these we may find after death, though it is then always a question how far the erosions may be the result of a post-mortem digestion.

(*b*) In **chronic gastritis** the mucous membrane of the stomach is atrophied, and the gastric wall may be much thinner than normal. At the same time the stomach itself is liable to be dilated. Dilatation of the stomach may proceed to extreme degrees, so that the viscus may contain quarts of fluid, and may extend, in the abdomen, as low as the umbilicus, or even lower. The condition is accompanied by somewhat definite symptoms which divide it from chronic gastritis clinically, but there is little doubt that many cases of dilatation of the stomach develop out of cases of chronic gastritis. This is, however, only the case with chronic dilatation. In some cases the dilatation is acute, and then the pathology is different, though what it is in these cases is largely a matter of conjecture.

(*c*) **Gastric ulcer.**—Ulcers of the stomach are of various kinds, and the most important, as well as the most extensive, are those which are found in connection with carcinoma of the organ. But it is not these ulcers which are meant when the term 'gastric ulcer' is used. By that term is always meant a non-malignant ulcer of very definite characters.

A gastric ulcer is a chronic condition. Although it is no doubt acute in its actual onset, there is little doubt that the ulcer as we see it at an operation or an autopsy is the ultimate expression of changes which have been going on for some time owing to the impediment in the way of repair that has been introduced by the movements of the stomach and the acid character of its contents.

The ulcer itself has a very characteristic shape. It is usually round, or approximately round; it is generally single, though two or three are sometimes found; its edges are clean cut, so that the ulcer has a 'punched-out' appearance; its walls shelve downwards, so that the ulcer is funnel-shaped, and its floor is generally made by the denuded muscular coat of the organ. It has a somewhat characteristic situation, for it is generally found in the smaller curvature of the stomach, midway between the cardiac and pyloric orifices, but somewhat nearer to the pyloric orifice, and it is generally placed on the posterior surface of the organ, although in a fair number of instances it is situated on the anterior surface. Its floor is almost always smooth, but in cases in which there has been hæmorrhage immediately before death we may find the open end of an artery on the floor, and perhaps a small amount of blood clot.

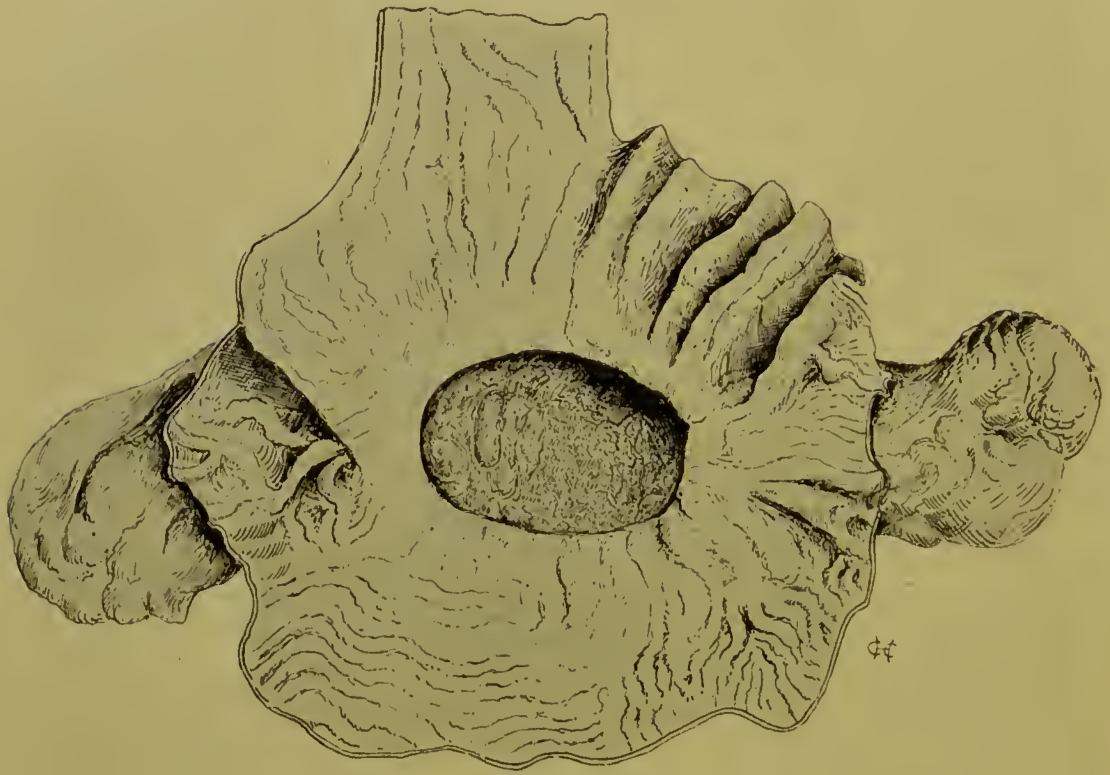


Fig. 93.—Simple Chronic Gastric Ulcer. × $\frac{2}{3}$.
The ulcer is oval, has sharp cut edges, and has the pancreas as its floor. The termination of the œsophagus is seen above and portions of the pancreas on the right and left sides of the figure.

Such is the appearance of a typical gastric ulcer, and it is remarkable how little individual cases vary from the type. The commonest variation consists in the fact that the ulceration proceeds further than the muscular coat of the stomach. The actual changes which are then produced depend upon circumstances. If the process is not very acute, the irritant action extends to the serous coat of the organ, and there leads to an adhesive inflammation which fixes the organ to the underlying parts. In this way the stomach may become attached to the liver or the pancreas, for example, and then, if the gastric ulceration proceeds, the floor of the ulcer may not be formed by any portion of the gastric wall at all, but by the viscus which has become adherent to the stomach. In the accompanying figure, for example, the floor of the ulcer was made by the pancreas itself. If, on the other hand, the formation of the ulcer has proceeded with so great a rapidity that time has not been given for the formation of adhesions, or of adhesions of sufficient resistance, the extension of the ulcer leads to a definite perforation of the stomach and the production of a peritonitis which is more extensive or more circumscribed according to circumstances.

In cases in which there has been a fair amount of adhesive peritonitis in the region of the ulcer before it perforated, the escaped gastric contents lead to the formation of a sub-diaphragmatic abscess. This abscess may be well localised, and it may be possible for it to be treated surgically. On the other hand, it may be accompanied by symptoms of an indefinite nature, and may first manifest itself with certainty by its rupture. In such cases the pus may be evacuated into the colon, or the pleural cavity, for example. In yet other cases in which the serous surface of the stomach in the neighbourhood of the ulcer has become adherent to the liver, the formation of pus takes place in this organ, and a ragged and extending abscess is produced.

Histologically there is nothing characteristic about a gastric ulcer. The floor is seen to be infiltrated with a number of leucocytes, and the actual tissue elements upon the floor are degenerated in character. The mucous membrane of the stomach up to the very edge of the ulcer is often completely normal. Collections of leucocytes are generally seen around the smaller blood-vessels, and the closeness with which the ulcerative process reaches to the arterioles lying in the muscular coat of the stomach is generally seen with great distinctness.

Like other ulcers, a gastric ulcer may become cicatrised. Under these circumstances we cannot but believe that the floor of the ulcer becomes altered by the formation of granulation tissue, though, as a matter of fact, we do not find cases in which this change is manifest. Either we have to deal with an ulcer which is devoid of any reparative changes or one in which repair is complete. In the latter case the former seat of the ulcer is shown by a depressed scar, and the gastric wall at this spot, though composed of firmer tissue than normal, is nevertheless considerably thinned. Contraction takes place to a varying extent. In most instances it is slight, and we are only able to distinguish the scar with difficulty and by a slight puckering and thickening of the serous surface of the stomach at one spot. But in other instances, and especially those in which the ulcer has been of large size, the cicatrisation is accompanied by marked changes in the shape of the organ. It is generally believed that the condition known as 'hour-glass' constriction of the stomach is due to the cicatrisation of a gastric ulcer. In such cases the stomach may become converted into a double sac, the communication between which is so small that it will barely admit the little finger. The seat of such a stenosis is almost always at a point midway between the cardiac and the pyloric orifices of the organ, and since the stenosed portion is at the same time thickened, the appearance of a second pyloric orifice is given.

In a few cases we meet with ulcers of the stomach in which one portion has undergone carcinomatous change. The ulcer in these instances has generally been close to the pyloric orifice, and the carcinomatous modification is characterised by the features that are peculiar to carcinoma of the pylorus. In these cases it is often difficult to decide whether the ulcer which is present has, or has not, been carcinomatous from the commencement. But in a certain number of cases the matter is beyond doubt, for we find that one end of the ulcer offers the histological features of a simple chronic gastric ulcer, while the other yields those of a typical carcinoma. In any case, however, the matter is one which the microscope alone can decide.

(2) **Congestion.**—Before leaving the more simple morbid conditions of the stomach, mention must be made of the change which is present in cases in which the entire gastric mucous membrane is the seat of chronic venous congestion. Such a condition is met with in a typical manner in cases of heart disease which have come to the state of cardiac failure owing to the occurrence of tricuspid regurgitation. The stomach is then found to be of a deep red colour, its mucous membrane swollen and covered by a thick and tenacious layer of mucus, and the rugæ very prominent. The histological characters of such a stomach have nothing peculiar beyond the existence of a very marked general congestion, and a catarrhal proliferation of the cells in the gastric glands. The change is one which is common to the entire gastro-intestinal tract, but it is especially noticeable in the stomach.

(3) **Carcinoma.**—Carcinoma of the stomach is generally met

with either at the cardiac or at the pyloric end. Unless the disease has spread from one or other of these situations, it is uncommon for the other parts of the stomach to be affected. The characters of the growths present in the two situations are very different.

Carcinoma of the **cardiac** end is generally extensive and soft. It is therefore accompanied by the formation of large ragged ulcers with raised edges, where the growth has undermined the mucous membrane, but has not, as yet, broken down. The thickness of the gastric wall at the situation of the growth, in spite of the fact that the centre of the ulcer lies well beneath the edges, is much increased. At the edges of the growth the stomach wall may be three or four times its normal thickness. The growth extends in all directions, so that it invades the lower part

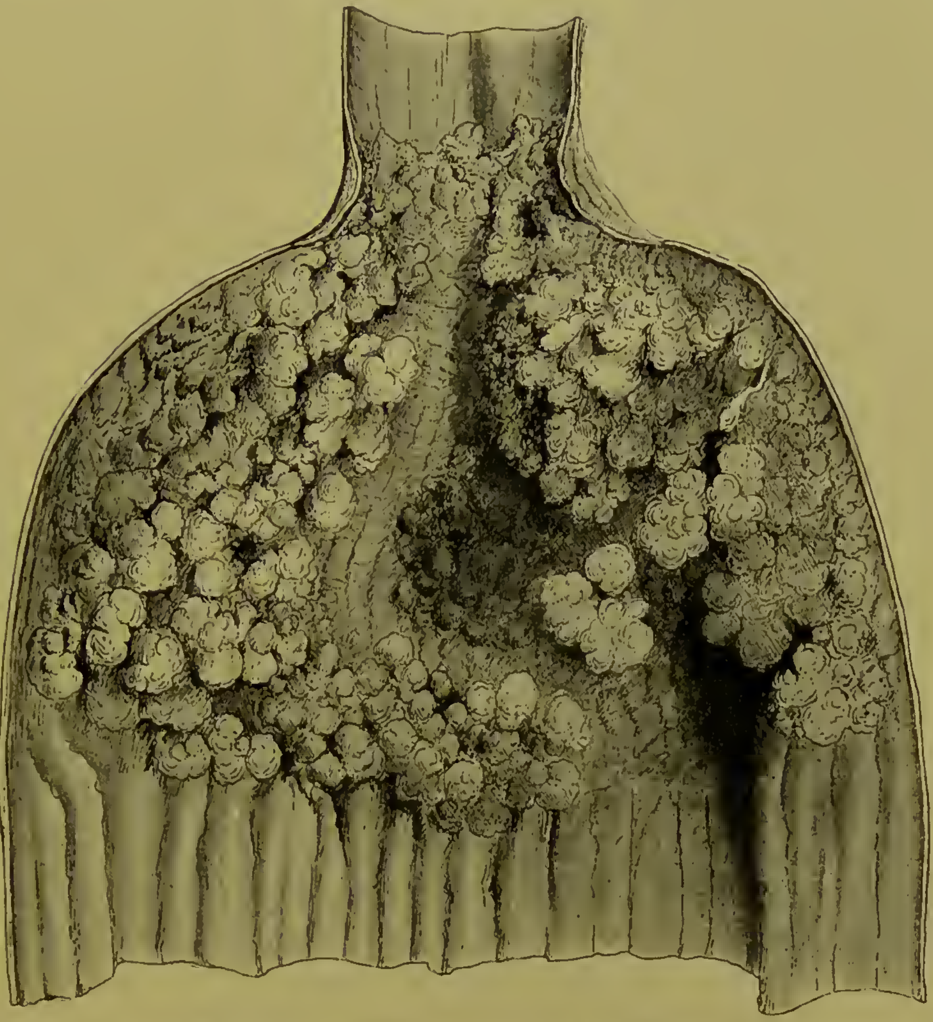


FIG. 94.—MALIGNANT DISEASE OF STOMACH (CARDIAC END.) × $\frac{2}{3}$.
At the cardiac end of the stomach and slightly encroaching upon the œsophagus is a polypose mass of carcinoma (spheroidal cell).

of the œsophagus on the one hand, and the fundus of the stomach on the other. Sometimes the growth contracts adhesions to the under surface of the liver before it has proceeded very far, and then it may invade the liver by way of the adhesions and lead to the formation of a large ragged cavity in the very substance of the organ. In these circumstances the gastric contents are placed in contact with the liver substance, and the formation of the ulcerated malignant cavity is furthered by the suppurative processes at work at the same time. At other times the growth involves the entire wall of the stomach, so that the viscus is converted into a ragged cavity with thickened walls. The actual dimension of the stomach cavity under these circumstances is apt to be very small.

Carcinoma of the **pylorus** differs considerably from the variety that has just been described. Instead of being voluminous, it is generally very circumscribed; instead of ulcerating freely, ulceration is generally inconspicuous or wanting entirely; instead of being a soft growth, it is dense and hard. As a rule, it encircles the sphincter pylori, growing into and replacing the muscle itself. From the outside a mass of carcinoma in this situation hardly gives the impression of being more than a moderately hypertrophied sphincter. At the same time there may be a few adhesions and irregularities that give a clue to the real nature of the change.

Both in the case of carcinoma of the cardiac end and in that of the pyloric end, we generally have to do with a spheroidal cell growth. The main difference between them lies in the relative amounts of fibrous tissue which enter into the composition of the growth. In the soft carcinoma of the cardiac end the amount of fibrous tissue is extremely small, while the number of cells is proportionately great. Carcinoma of the pylorus, on the other hand, consists so largely of fibrous tissue, and so few cells are present, that the growth has been called **scirrhus.** The highly cellular growth of the cardiac end has many of the appearances of an adenoma. That is to say, it consists of a number of alveoli which are filled with epithelial cells. It is very liable to degenerative changes, so that it is only by taking a portion that is far removed from the centre of the growth that it is possible to form an opinion from microscopical examination as to the exact nature of the growth. From its appearances this variety of carcinoma of the stomach is sometimes termed *malignant adenoma.*

Often the histological appearances of a carcinoma of the stomach, and particularly one of the cardiac end, are not so conclusive that it is possible to diagnose the type of the growth without difficulty. The reason of this may lie in the extent to which degeneration has advanced, but it is more likely to depend upon the fact that the actual characters of the growth are not clear. In a certain number of cases we meet with carcinomata of the truly columnar-cell type, but in a larger number we meet with a variety which we are unable to assign to either the spheroidal-cell or the columnar-cell type with sureness, and which we speak of as 'transitional.' In such cases we find at one spot alveoli that are lined by a layer of epithelial cells, as in the true columnar carcinoma, but the cells are more of the spheroidal type; at another spot we find definite alveoli filled entirely with cells of the strictly spheroidal type, and producing a picture identical with that of a typical spheroidal-cell carcinoma such as we meet with in the breast.

In very rare instances we meet with a condition in which the entire wall of the stomach is infiltrated with a squamous-cell carcinoma. The growth is in such instances somewhat soft and is likely to have undergone considerable degeneration. As to the origin of this variety of carcinoma the most obvious suggestion is that it represents a carcinoma of the œsophagus which has commenced at the very end of the tube, and has spread over the stomach instead of up the œsophagus. That this may be the case is incontestable, but it is remarkable how the growths stop short at the junction of œsophagus and stomach. Nevertheless, if this be not the true reason, it is most difficult to suggest any other.

As a result of the presence of carcinoma in the wall of the stomach such portions of the gastric wall as are not themselves infiltrated by the growth undergo change. This is particularly noticeable in the case of pyloric carcinoma. For then the presence of the growth and its physical characters lead to the occurrence of a stenosis of the stomach at the pylorus. The muscular walls of the stomach therefore undergo hypertrophy, and the increase in thickness may be to as much as half an inch. This hypertrophy of the muscular coat is one of the most characteristic features of carcinoma of the pylorus. As might be expected, it is not nearly so evident in carcinoma of the cardiac end, though even in this disease we generally find that the muscle has undergone a certain amount of hypertrophy.

In very rare cases we meet with **sarcomata** of the stomach. The growth then presents characters which it is impossible to distinguish, except by the microscope, from a soft spheroidal-cell carcinoma.

In cases of **lymphadenoma** we sometimes find masses of lymphadenomatous tissue in the wall of the stomach. Cases of this description, and cases in which other varieties of new-growth are found in the stomach, are so rare, that their consideration need not detain us here.

(4) **Effects of corrosive poisons.**—It has been thought better to consider here the entire list of changes produced in the alimentary tract by the swallowing of corrosive poisons, because these effects, although manifested in some degree upon the mouth, œsophagus, and intestines, nevertheless are seen in their severest form in the case of the stomach.

The changes may generally be summed up in the statement that the epithelial surface is entirely disorganised, and tends to strip off in flakes, in regions in which the action of the corrosive has been short, as in the mouth and the œsophagus, and that there is a complete destruction, with admixture of altered blood, in the case of those parts, such as the stomach and intestine, upon which the action of the corrosive has been more prolonged.

About the mouth there are often yellow or brown stains due to the immediate action of the corrosive. These are generally visible on the lips, and there may be here a certain amount of destruction of the epithelium with subsequent drying and formation of a thin crust. In the mouth itself the same appearances are to be observed, but owing to the rapidity of the passage of the fluid through the pharynx the changes here are usually less well marked. The œsophagus generally shows a very characteristic change. Its epithelial covering is thrown into numerous longitudinal folds, is desquamating in places, and in any case can be removed in large flakes with the utmost readiness, and the entire epithelium has a peculiar satiny appearance which is unlike that present in any other condition. This satiny appearance extends throughout the whole length of the tube and ends abruptly at the cardiac orifice. It is seen without distinction in cases of poisoning by any kind of corrosive, but is perhaps best marked when the swallowed poison has been carbolic acid.

In the stomach the changes vary somewhat according to the nature of the poison. When it is such a substance as strong hydrochloric or nitric or sulphuric acid, the gastric wall is often completely disorganised at the situation at which the acid has longest been in contact—viz. at the fundus—and a ragged hole is made through which the gastric contents escape into the peritoneal cavity. At the same time such of the mucous membrane as is not totally destroyed is tumid and black from the presence in it of large amounts of altered blood. In some cases the corrosive leads to a contraction of the gastric vessels at its first contact with the mucous membrane, and then the lining membrane of the stomach is of a dead-white colour in places. When carbolic acid has been swallowed, the mucous membrane of the stomach is tumid and thrown into folds, and white patches are usually present, but the colour of the gastric wall itself is of a deep reddish-purple colour. The wall of the stomach, too, is of a leathery consistency, and perforation is less common than with the stronger acids. The differences between the effects of strong acids and of strong alkalies upon the stomach are very small.

The effects of swallowing corrosive fluids upon the intestines are very different in different cases. The principal reason for this lies in the length of time which elapses between swallowing of the corrosive and death. But this does not explain everything. It appears that in some cases an attempt is made by the mucous membrane of the intestine to eliminate the poison. Thus we find that the effects of corrosive sublimate when taken by the mouth in large doses are to be seen clearly in the lower part of the large intestine, the upper portion remaining free. In the case of this poison the anatomical change consists in a severe ulceration of the mucous membrane of the rectum. In other cases there is no doubt that the intestinal changes depend upon the immediate action of the poisonous corrosive fluid upon the mucous membrane as it travels along the intestine. Thus in the case of poisoning by carbolic acid we generally find a modification of the intestinal mucous membrane exactly similar to that which is present in the stomach. It is thickened, leathery, deep red or purple, and there are superficial destructions of the mucous surface. A remarkable point in connection with this poison is that the intestinal changes are present over a certain length of the intestine and then stop with the greatest abruptness. When death has occurred two hours after swallowing the poison, changes may be seen for as much as seven feet down the small intestine. Over this length of gut hardly any difference is to be seen between the changes at the commencement and those at the point at which the changes suddenly cease. Microscopically the altered mucous membrane only shows a profound disorganisation, together with the presence of numerous foci of hæmorrhage. The blood corpuscles in the hæmorrhages are usually much broken down.

(5) **Post-mortem digestion.**—Before leaving the consideration of the morbid changes of the stomach mention must be made of a change which is not definitely pathological, but which may be

the cause of difficulty at a post-mortem examination. It is sometimes found that a ragged hole is present at the fundus of the organ. This hole is apt to be of large size, and is more commonly found in the case of persons who have died suddenly as the result of some accident while full digestion was going on. There is no doubt that the condition is one of post-mortem digestion of the gastric wall. That the change was produced after death is shown by the complete absence of any evidences of inflammation or of hæmorrhage, while the fact that half-digested food is present in the stomach and has passed into the peritoneal cavity through the hole in the stomach, is highly suggestive of the nature of the process which has been at work. The change, however, is by no means a common one. As might be expected, it is more commonly seen in warm than in cold weather.

SECTION IX

THE DIGESTIVE TRACT—continued

(3) THE INTESTINES AND PERITONEUM

A.—THE INTESTINES

Morbid conditions of the intestines are far more commonly local than general, as might be expected from the length of the tract in question.

(1) **Atrophy.**—Of strictly general conditions, the only one of pathological importance is **atrophy**, and even then it is by no means in all cases, as will appear later, that the atrophy is general. In old age, however, it is customary to find that the walls of the intestine are thinner than normal, while there is also present that **pigmentary deposition** which is so frequently associated with senile atrophy. The atrophic change is manifested by a greater translucency than normal of the gut. It affects principally the small intestine, affects all the coats, but particularly the muscular. The pigment is deposited in the muscular bundles, and frequently in the muscular fibres themselves. It is of a pale yellow colour, and may fail to give evidence of its presence, even when it exists in large quantities, unless the microscope is resorted to. The entire change has close analogies with brown atrophy of the heart.

In the very young, and especially in the case of infants who have died of continued diarrhœa, we may also find an atrophy of the intestine. Here, as before, the change is liable to be manifested macroscopically by a greater translucency of the gut. But it does not depend upon a general thinning of all the coats of the gut, but rather upon a thinning of the mucous coat alone. Microscopically such cases may afford little evidence beyond the impression that the mucous membrane is less extensive, that the tubular glands are less numerous and shorter than normal, and that the lymphoid tissue is present in abnormally small amount.

(2) **Malformations and malpositions.** (*a*) **Meckel's diverticulum.** --This malformation consists in a persistence of the omphalo-mesenteric duct, which remains and develops into a diverticulum of the small intestine. This diverticulum, when present, opens into the small intestine at a point about two feet above the ileo-cæcal valve, it is usually of much the same diameter as the gut itself, and it ends blindly in most cases. In those cases in which it does not end blindly, the diverticulum opens at the umbilicus, forming a fæcal fistula. Far more commonly the diverticulum is not even attached to the umbilicus by a fibrous cord, but lies free in the abdominal cavity. The length of the diverticulum varies considerably. In some cases nothing more than a dimple is present in the wall of the gut, in the majority the process is about an inch in length, but sometimes it is as much as three or four inches. The attachment to the wall of the intestine is opposite to the mesentery.

(*b*) **Atresia ani.**—This is a form of congenital malformation which is met with in new-born infants. In the process of development the blind end of the hind gut is normally met by a process dipping inwards from the epidermal surface and caused by an invagination of the skin at the point of the future anus. When these two processes have met the partitions between them are absorbed, and the external opening of the gut is established. But sometimes there is a defect in development. Either the epidermal invagination does not take place, or the process does not reach up high enough to meet the blind process of the hind gut, or the partition between the two blind ends is not absorbed, or the hind gut does not reach far enough down. Under any of these circumstances an external opening to the gut is wanting, and unless surgery can repair the defect, life is impossible. This malformation is met with about as frequently as a Meckel's diverticulum.

Of far more importance from a practical point of view than the malformations are the malpositions of the intestines. For these are responsible for a very large number of those conditions which are summed up under the name of 'intestinal obstruction.' Some of these malpositions are due to malformations of parts other than the intestines, some are due to accident, while some are brought about by the effects of disease whether in the intestines or in parts outside them.

This part of pathology trenches very closely upon the domain of surgery, and therefore it will not be necessary to refer to it in detail, but the conditions themselves, and even more the changes which occur in the intestines when the malpositions are present, are distinctly pathological, and therefore call for some remark here.

The chief malpositions of the intestines are those which constitute the conditions known as **hernia**, **intussusception**, and **volvulus**. Each of these is sufficiently important to merit special notice.

(*c*) **Hernia.**—By the term **hernia** it is not necessarily meant that a morbid condition of the *intestines* is concerned. The term is applied to many other conditions, such as hernia cerebri, hernia testis, while we may have a hernia of the lung and so on. But in all these cases we have one constant factor in the point that a herniated part is one which is not contained in the cavity which is normal to it. Thus a hernia of the lung occurs if the lung, or a portion of it, is found in the peritoneal cavity owing to a congenital deficiency of the diaphragm. When the term is unqualified, however, by the name of the organ or tissue involved, it is always taken to refer to a hernia of intestine or of omentum.

Hernia may be found in several situations, the most usual of which are those at which there is some congenital or anatomical weakness of the abdominal wall. Thus a very large majority of all forms of hernia occur by passage of a portion of intestine through the internal inguinal ring into the inguinal canal, and thence into the scrotum. This is particularly the case in the male, owing to the large size of the spermatic cord and the inguinal ring. The next most common situation is through the femoral ring, and this is the commonest variety of hernia met with in the female. Then, in order of frequency, come umbilical herniæ in which the protrusion takes place at the umbilicus or in its neighbourhood. Herniæ through the obturator foramen, through the sciatic notch, through the diaphragm, &c., are known to occur, but are decidedly rare.

Under ordinary circumstances when a knuckle of intestine has passed into a hernial sac, it is possible to bring about the return of the portion of gut by posture or manipulation. Under these circumstances the hernia is said to be **reducible**. But subsequently to its formation an intestinal, omental, or any other variety of hernia may undergo such changes that it becomes completely irreducible. These changes may be of different kinds. In the case of the '**irreducible** hernia' of the surgeon, the serous wall of the intestine has contracted adhesions to the serous wall of the sac, as the result of a slow form of inflammation which has probably been quite unaccompanied by symptoms. In the other variety, in which it is impossible to reduce the hernia, the condition is due to **strangulation**. Here some modification has been introduced in the conditions that formerly obtained, and the circulation is progressively impeded in the mesentery of the portion of gut within the hernia, or in the portion of omentum, if the hernia be of this kind, until it is brought to a complete standstill. The included portion of tissue then becomes deeply congested, a blood-stained fluid is poured out into the cavity of the sac (and this at the same time increases the embarrassment of the local circulation), and unless the constriction is divided surgically, the portion of included tissue rapidly becomes gangrenous.

It does not, of course, follow that the tissue of a hernia which becomes inflamed of necessity passes on to a condition of complete strangulation or of gangrene. Although this is very likely to be the case, it is clear that the amount of congestion and of exudation, and the diameter of the ring through which the hernia has passed, may be such that the vascular obstruction in the herniated tissues is not sufficient to cause them to become strangulated. Under these circumstances the condition is one of an *inflamed* hernia alone.

(*d*) **Intussusception.**—In intussusception an invagination of one portion of intestine takes place into that which lies immediately below it. The result of the invagination is that at the seat of the intussusception three layers of bowel are present lying within one another. On the outside is the *receiving* portion which has the serous surface directed outwards as under normal circumstances. Internal to this comes a layer which has the mucous surface directed outwards, so that the mucous surfaces of this—the *returning* layer—and the receiving layer are in contact. Internal to the receiving and the returning layers, is a layer of gut—the *entering* layer—which has its serous surface outwards as normally, and in contact with the serous surface of the returning layer. The entering layer corresponds to the upper portion of the gut, while the receiving layer corresponds to a lower portion. The returning layer always formed at one time a portion of the receiving layer.

The formation of an intussusception cannot be without important effects upon the circulation of the enclosed gut. For it is clear that the mesentery must pass with the intussuscepted bowel. At first it may be easily possible to pull the entering layer out of the receiving layer and thus reduce the intussusception. But after the malposition has been in existence for a short time the obstruction of the mesenteric blood-vessels leads to a great congestion of the mucous membrane of both the entering and the returning layers. This congestion may be sufficient to lead to gangrene of the included portion of gut. In other cases the inflammation which is set up between the two serous surfaces of the entering and the returning layers is sufficient to lead to adhesion of these surfaces.

The occurrence of gangrene with an intusception is the natural method of cure of the condition. For there occurs an adhesive inflammation at the point where the serous surface of the entering portion comes into contact with the serous surface of the receiving portion, viz. at the highest part of the entire intussusception, and this, going on to the formation of new fibrous tissue, provides for the continuity of the gut when the gangrenous entering and returning portions have become separated and cast off. This natural method of cure is a very rare one, but cases have been known in which as much as nine inches of intussuscepted gut have been cast off as a slough, and recovery has taken place. More commonly the patient succumbs to the acute intestinal obstruction which the intussusception produces, unless surgical methods are adopted soon and successfully.

(*e*) **Volvulus.**—A volvulus is a twisting of a loop of intestine upon itself at its mesenteric attachment. At first the twist is a simple one, but in most cases it is found that the number of turns is three or four. The changes that are produced depend upon the interference in the circulation which the twisting induces. As a rule, the coils of the twist are not very tight, and therefore the vascular obstruction affects the veins rather than the arteries. In consequence the portion of gut concerned becomes intensely engorged, and ultimately, if the twist be not reduced, a condition of moist gangrene results. There is nothing of special pathological importance which causes the subsequent changes of a volvulus to differ from those which occur either in a strangulated hernia or in an intussusception.

(3) **Inflammation.**—Inflammatory conditions of the intestines may be conveniently divided into those which are not accompanied by ulceration and those which are. Conditions accompanied by ulceration form by far the larger class, and even in the case of those which are not usually associated with ulceration, small erosions may often be found if especial care is taken in the examination, and if the inflammation itself is of more than a very slight degree of severity.

(A) **Inflammation unaccompanied by ulceration.**—The conditions which constitute this class are comprised under the name of **enteritis**, on the one hand, and certain specific inflammations on the other. Of these specific inflammations cholera is the best example.

(*a*) **Enteritis** is a condition which chiefly affects very young children. It is associated with diarrhœa as its principal symptom, but the anatomical and histological changes present in the intestines of a child that has died of enteritis are very meagre. As a rule we find little more than a congestion of the mucous membrane, particularly in the upper portion of the tract. This congestion is far better recognised macroscopically than microscopically. At the same time there is probably evidence of a catarrhal inflammation of the mucous membrane in the presence of an inordinate amount of mucus on the surface of the mucous membrane and in the intestinal contents. Blood may be extravasated, but this is not usually the case. In very severe cases small erosions of the mucosa may be found.

When the disease affects adults, the changes to which it gives rise are different from those occurring in children. Thus it is common for the condition to arise as an extension of an acute gastritis, and then the inflammation is definitely catarrhal. It is associated with considerable swelling of the mucous membrane of the duodenum, and, this extending to the orifice of the common bile duct and frequently up its course, a jaundice of rapid onset is produced. In children, on the other hand, the condition is not so definitely an extension of a gastritis, is not confined to the duodenum, but affects the entire length of the small intestine, and is but rarely the cause of jaundice.

In very rare cases the inflammation is so severe that it leads to a superficial coagulation necrosis of considerable portions of the intestinal mucous membrane. Under these circumstances the mucous surface is covered with a somewhat adherent whitish membrane. It is cases of this description which have been termed ‘diphtheritic enteritis’ by German authors, but the name is a bad one in that the condition has nothing whatever to do with the disease caused by the diphtheritic bacillus.

A special variety of enteritis is caused by the ingestion of certain kinds of food. Not all varieties of food-poisoning are characterised by the production of an enteritis, but in a considerable number of cases a condition is found after death of which an intense enteritis is the most prominent feature. This enteritis is generally associated with the presence of a micro-organism (*B. enteritidis* of Gaertner) which seems to be causally related to the condition. In many of its characters this micro-organism is closely allied to the typhoid bacillus, but the two are not identical.

(*b*) **Cholera asiatica** is a condition in which there is a general acute inflammation of the mucous membrane of the entire intestine, with the outpouring into the lumen of a large quantity of watery fluid in which small portions of mucus may be found. The disease is associated with the presence of a large number of curved rods (vibrios), and it is probable that these stand in a causal relation to the disease. If the patient with cholera dies at an early stage in the disease, the mucous membrane of the small intestine is found to be injected, swollen, of a pink colour, and very soft. Here and there hæmorrhages may be present. So far as the epithelium is concerned at an early stage, it is in a condition of desquamation and mucous degeneration. At a later stage the epithelium is entirely lost and mixes with the fluid in the lumen. The connective tissue is infiltrated with considerable numbers of round cells, and the serous coat is similarly affected. In most cases the ileum is more affected than other parts of the intestine, and in early cases the large intestine appears to be practically unchanged. If death ensues at a later stage in the disease, the amount of fluid in the lumen is less, far less watery, tinged with bile, and it may be with blood. The intestinal wall may be smooth and pale or injected, but in any case the changes are less marked than when the disease proves fatal at an early stage. Sometimes the mucous membrane is detached in flakes, and then we have a condition bordering on the varieties of inflammation with ulceration.

(*c*) **Membranous colitis.**—This condition is characterised by the passage in the stools of large amounts of mucus, or material which has undergone mucoid degeneration, in the form of flakes or shreds of a gelatinous and colourless substance. These flakes vary considerably in size; as a rule, they are about the size of the finger nail, but sometimes large casts of the intestine are discharged, and these may be six or eight inches in length. On microscopic examination the material does not appear to be entirely homogeneous, but shows minute circular spots which, in some instances, stain fairly well with basic dyes and therefore suggest nuclei, and in other instances do not stain at all, but appear to be pits or actual spaces in the substance of the material. It has been supposed that these pits correspond to the orifices of the tubular glands of the intestine, and that the entire gelatinous mass has at one time been attached to the mucous membrane of the gut, and has become detached as a cast. This view is in the highest degree probable.

So far as the condition of the intestine is concerned in which this discharge of mucous casts and flakes is the prominent feature, it is impossible to speak with certainty. We are accustomed to hold that the mucous membrane of the lower part of the colon is in a condition of catarrhal inflammation, and probably we are fairly correct. But the patients who manifest the condition are of the most varied kind and age, and the condition itself persists for so long a time without leading to severe symptoms, and particularly is not itself likely to be fatal, that we have really no anatomical or histological data upon which to go in forming our opinion as to the actual nature of the lesion by which the condition is occasioned.

(B) **Inflammation in which ulceration is present.**—Inflammatory conditions of this kind are the most important as well as the commonest to be met with in the intestine. At the same time the ætiological factors which underlie them are of most diverse kind. They include such conditions as typhoid fever, tuberculosis, syphilis, dysentery, actinomycosis, &c. It will be necessary to refer to them individually, although the pathological processes underlying them all are the same, because the macroscopic pictures presented by the various conditions are so different. It will be convenient if we describe them according to the part of the intestinal tract which they are most likely to affect.

(*a*) **Duodenal ulcer.**—This condition is closely allied to gastric ulcer, so far as shape and the sharp-cut character of the edges are concerned. They are in almost all cases single, and situated on the posterior wall of the duodenum in its first part. As a matter of fact they generally impinge upon the sphincter pylori. In one point there is a great contrast between duodenal and gastric ulcers; for whereas gastric ulcer is generally found in women (apart from that variety which is dependent upon chronic alcoholism, and which may be found in either sex), duodenal ulcers are far more commonly met with in men.

Histologically the appearances are those of a process in which the ulcerative changes entirely dominate the general inflammatory changes. In other words, we meet with marked evidence of the destruction of tissue, but the small cell infiltration of surrounding tissue, the congestion, and the evidence of inflammatory exudation, are relatively very slight.

(*b*) **Typhoid fever.**—Typhoid or enteric fever is a general infective disease in which the principal lesions are found in the intestine, although they are not confined to this region. We have already described the characters of the typhoid inflammation (p. 95), so that in this place we have only to consider the macroscopic characters of the condition.

In typhoid fever the lymphoid tissue of the intestine is the constituent of the wall of the gut that bears the brunt of the infection. The characteristic changes are seen in the Peyer's patches and in the solitary follicles. At an early stage in the disease these appear swollen, while the serous surface of the intestine lying beneath them is markedly congested. In this congestion lies the difference between a simple hyperplasia of the lymphoid tissue, such as is shown in fig. 3, and the inflammatory swelling of the infective disease. In course of time the entire follicle dies and is cast off as a slough, leaving the characteristic typhoid ulcer.

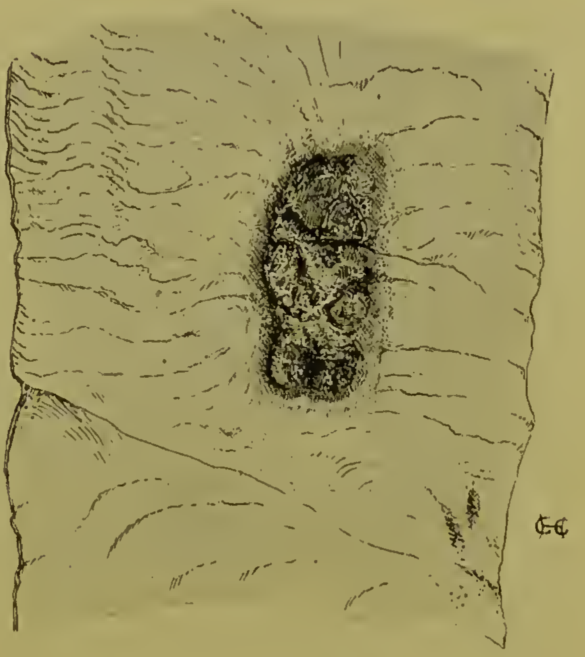


Fig. 95.—Typhoid Ulcer with Slough attached. Natural Size.

The ulcer is in the longitudinal axis of the ileum and affects an entire Peyer's patch.

The typhoid ulcer, taking as an example one which has formed at the site of a Peyer's patch, is situated on the surface of the intestine opposite to the mesenteric attachment. Its long axis lies in the long axis of the gut, and its edges are sharply cut. Its floor is made by the muscular coat of the intestine. An ulcer formed at the site of a solitary follicle is circular, much smaller, its edges are also sharply cut, but its position is not confined to that surface of the intestine which is opposite to the mesenteric attachment.

Owing to the fact that the Peyer's patches are only found in the ileum, the characteristic lesion of typhoid fever is only seen in this situation also. Nevertheless the fact that the solitary follicles share in the disease accounts for the occasional presence of small ulcers in the large intestine. Ulcers of the large intestine are present in perhaps a quarter of the cases. Owing to the disposition of the Peyer's patches in the ileum, it follows that the effect of typhoid fever is more and more manifest as one passes down the small intestine, and is most intense at and about the ileo-cæcal valve.

Apparently the invasion of the lymphoid tissue of the intestine in typhoid fever does not take place at one and the same time throughout the length of the gut. For it is always found that the changes are most intense in the immediate neighbourhood of the valve and diminish in severity as one passes away from it. Thus we may meet with complete separation of the sloughs at the valve, attachment of the sloughs a little higher up, and still higher we are certain to find solitary follicles, if not Peyer's patches, which are only in a condition of inflammatory swelling.

The formation of an ulcer does not necessarily terminate the effects of the typhoid infection. It is clear that the amount of tissue which separates the lumen of the gut from the peritoneal cavity when the ulcer is fully formed is very small. Hence any slight extension of the ulcer in depth is liable to be accompanied by one of two accidents. When the ulceration is affecting the muscular coat, it may easily affect the wall of one of the arteries that run in this coat and lead to a severe hæmorrhage. On the other hand, the ulceration may pass beyond the muscular coat and lead to complete perforation of the bowel. Under the latter circumstances a portion of the intestinal contents is voided into the peritoneal cavity, and induces a peritonitis which is localised or generalised according to circumstances. As a matter of fact, the entire process is so rapid in the whole disease that general peritonitis is the more common sequel of perforation. Under all conditions, however, in which perforation occurs, a considerable deposition of fibrin takes place on the serous surface of the gut in the neighbourhood of the perforation. When typhoid ulcers heal, they do so by the formation of cicatrices in the usual way. These cicatrices contract in course of time, but since they are placed in the long axis of the gut they do not occasion any stenosis of importance. There is, therefore, no especial tendency for an attack of typhoid fever to be followed by intestinal obstruction.

(*c*) **Tuberculosis.**—It will be convenient to refer to tuberculosis of the intestine in this place, since it has many points of resemblance and of contrast to typhoid fever.

When tuberculosis affects the intestine, as distinguished from the peritoneum covering the intestine, it is almost always secondary to tuberculosis of the lungs. The first manifestation of the lesion consists in the formation of a small swelling in the mucous membrane. This rapidly caseates and breaks down into a small ulcer. By the formation of crops of small caseating tuberculous nodules in the periphery of this ulcer the local disease spreads and the extent of the ulcer increases. The process is therefore similar in all respects to the tuberculous process in other parts of the body. The infective process tends to spread by the lymphatics, and therefore it is common to find, on examining the serous surface of the gut opposite to the situation of the ulcer, a series of miliary tubercles which tend to lie in lines reaching round the intestine to its mesenteric attachment.

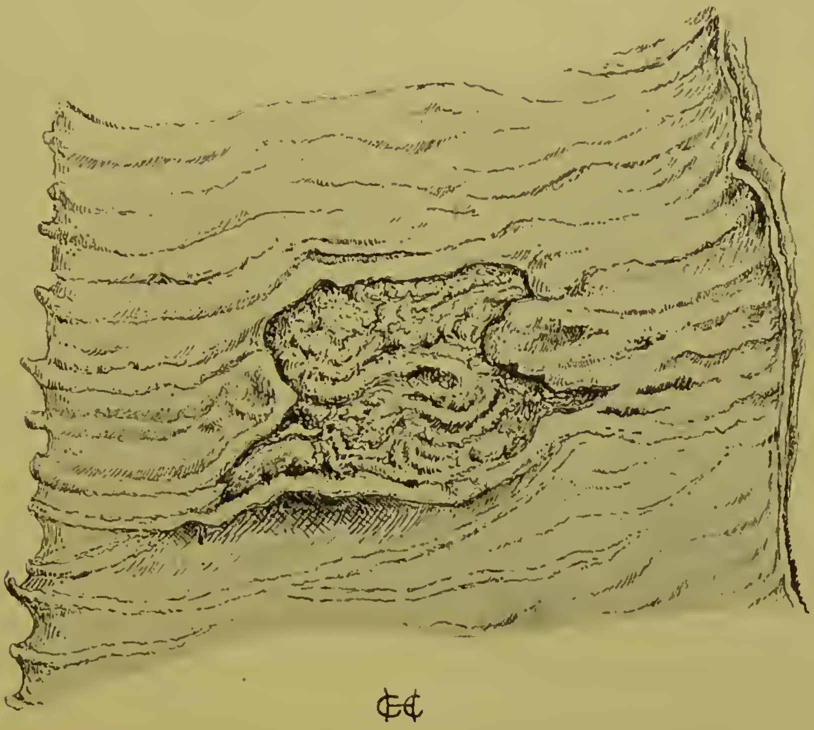


Fig. 96.—Tuberculous Ulcer. Natural Size.

From the jejunum. The ulcer is arranged circularly to the gut, is irregular in shape, has a ragged floor and thickened overhanging edges.

Tuberculous ulcers are of very different sizes. Some may be almost microscopic, others may be as large as a five-shilling piece. There is great reason to believe that they are the result of infection by swallowed tuberculous sputum in the majority of cases, and therefore the situations at which the ulcers are formed are determined largely by the situations at which it is possible for the sputum to become arrested. The chief point at which this can occur is the ileo-cæcal valve, and hence it is usual to find tuberculous ulceration most extensive in this situation. The lower part of the ileum is also a common seat for the ulcers, but they may be found high up in the jejunum or even in the duodenum in rare cases. In the large intestine they also occur, but are less common and are usually smaller. To the latter statement an exception must be made in the case of tuberculous ulceration of the rectum, which is usually extensive, and to the consideration of which we have to return later.

Tuberculous ulcers have a general tendency to be arranged around the gut, in this point offering a contrast to typhoid ulcers. But it must be allowed that the statements made on this point are not borne out by facts so fully as might appear from the dogmatic nature of the statement itself. As a matter of fact, it is quite as common to meet with tuberculous ulcers which have a long axis in the long axis of the gut as in the short. So much is this the case, that if attention is paid to the direction of the ulcers alone, and the other characters are ignored, serious mistakes may be made between tuberculous and typhoid ulceration. If attention be paid to the other characters of the lesions, it is almost impossible to mistake the one for the other.

The tuberculous ulcer has an overhanging edge due to the fact that the caseation and breaking down of the tubercles take place beneath the mucous membrane, and the contents of the tiny tuberculous abscess are subsequently discharged into the lumen of the gut. This method of formation of the ulcer is in marked contrast to that which leads to the formation of the typhoid ulcer, and accounts for the differences in the character of their edges.

(*d*) **Appendicitis.**—The vermiform appendix is liable to be affected with a form of inflammation that is very often associated with ulceration and even with gangrene. So generally is the disease localised to this part of the intestine and to the extra-intestinal tissues in the right iliac fossa, that the symptoms caused by the lesion are sufficiently distinct from those occurring in other forms of intestinal disease to erect appendicitis into a separate entity.

In its earliest form appendicitis is not necessarily accompanied by ulceration. On the contrary, it consists in a general inflammatory swelling of the lymphoid tissue which constitutes the bulk of the appendix itself. This inflammation is associated with swelling of the mucous membrane and the outpouring of a mucous secretion. The swelling of the mucosa is sufficient to block up the orifice of the appendix. The wall of the appendix itself is infiltrated with exudation fluid and a large number of migrated leucocytes. At the same time its vessels are engorged with blood. The inflammation extends to the tissues surrounding it, and the appendix itself becomes bound down in the iliac fossa by fibrin. The subsequent changes differ according to circumstances. In a large number of cases the inflammation recedes, and the ultimate result is merely a little thickening of the tissues concerned, with the formation of a few local adhesions. Under these circumstances the appendicitis is likely to be recurring. In other cases the inflammation goes on to the formation of an abscess (pericæcal or perityphlitic) which may burst into the general peritoneal cavity or may make its way through the tissues of the abdominal wall and burst externally.

A somewhat special variety of appendicitis is that which, from the severity of its symptoms and the rapidity with which they come on, has earned the appellation 'fulminating.' In it the inflammation proceeds at once to the gangrenous stage, and occasions general peritonitis by the escape of fæcal material through the ulcerated end of the appendix. In these cases there is no time for the formation of adhesions, and at the operation, or the autopsy, the appendix is found lying in a pool of pus and fæcal material. Usually the gangrene affects the tip of the appendix, but sometimes it occurs on one side, and in a few cases the entire appendix may be found lying entirely separated from the rest of the intestine, as the result of a gangrene which has occurred at its base.

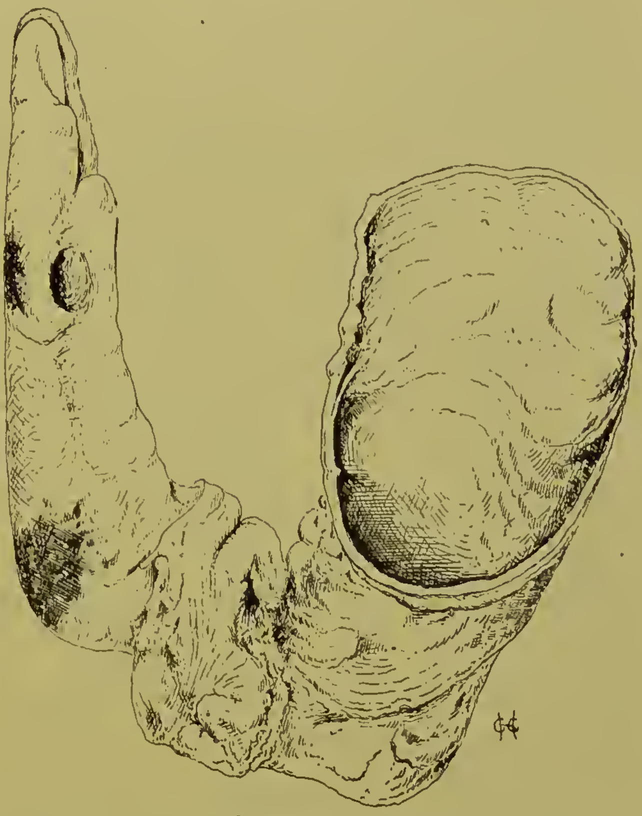


FIG. 97.—GANGRENOUS APPENDICITIS. NATURAL SIZE.

Two black patches of gangrene and one perforation of the appendix are visible. The perforation being situated laterally, is in a somewhat uncommon position; more commonly it occurs at the tip.

In many instances small hard bodies are found in the interior of the appendix or in the abscess cavity around it. These bodies have been compared to cherry-stones, but though the resemblance is often considerable, they actually consist of desquamated and compressed epithelial cells, together with a certain amount of mucus, fæcal material, and a variable number of micro-organisms. They have probably been formed *in situ*, and have not become accidentally lodged in the appendix, as used to be supposed.

The actual cause of the ordinary forms of appendicitis is quite unknown ; probably, indeed, the causes are many. It is, however, known that one variety of appendicitis is due to actinomycosis. In these cases we cannot but believe that the irritant has been introduced by the mouth and has become lodged accidentally in the appendix. The character of this variety of the disease is not usually recognised until it is found that the pus contains the small spherical grains of the actinomyces fungus. So far as the character of the inflammation produced is concerned, it tends to be somewhat more chronic than the ordinary variety, and always culminates in the formation of a perityphlitic abscess.

In the case of morbid conditions that have hitherto been mentioned, although the large intestine may be to some degree affected, the degree is always a very minor one. In those about to be described, on the contrary, the large intestine is affected to the practical exclusion of the small.

(*e*) **Ulcerative colitis.**—The condition which is known by this name is one of the most severe of all intestinal lesions. It is characterised by the presence of an extreme degree of ulceration throughout the colon. The characters of individual cases differ somewhat. In one case we find that the wall of the gut is thickened by inflammatory material, while the mucous membrane is in shreds. In another the wall of the colon is thin and adherent to the surrounding tissues, and tears at the least attempt to remove it at the autopsy. In yet another the gut will hardly hold together, owing to the innumerable and enormous rents that are present in the wall. Nevertheless all the cases agree in the fact that the mucous membrane is in shreds.

The wall of the gut may be quite pale at the autopsy, but more commonly it is of a dark slate colour owing to the changes which have taken place in the blood that is extravasated as the result of the ulceration. Microscopically the wall of the gut shows the most profound changes. The mucous membrane is in most places wanting, and where it is present it is in a gangrenous condition. Numerous hæmorrhages have taken place in the muscular coat, and such vessels as are present give evidence of a great congestion. Numbers of bacteria are present in the thickness of the remaining portion of the intestinal wall.

Concerning the ætiology of the condition it is impossible to say more than that it is probable that it depends upon some intense bacterial inflammation. Its relation to dysentery, with which it has many relationships, is quite undetermined. It is also uncertain whether several intrinsically different conditions are included under the one name. At most it can be said that the name by which the condition has been called is justified to the fullest extent. One of the most remarkable points in connection with the disease lies in the enormous number of rents that are present in some cases. These rents have been formed some time before death, there can be no doubt. They do not lead to a general peritonitis, but why this is so is a complete mystery.

The disease occurs sporadically, and it is this variety with which we meet in general hospitals. It also occurs in small epidemics, particularly in asylums for the insane; in the latter case a certain number of patients manifest a condition less severe than that which has been described above, but the disease is always one of the most severe scourges to which asylums are liable.

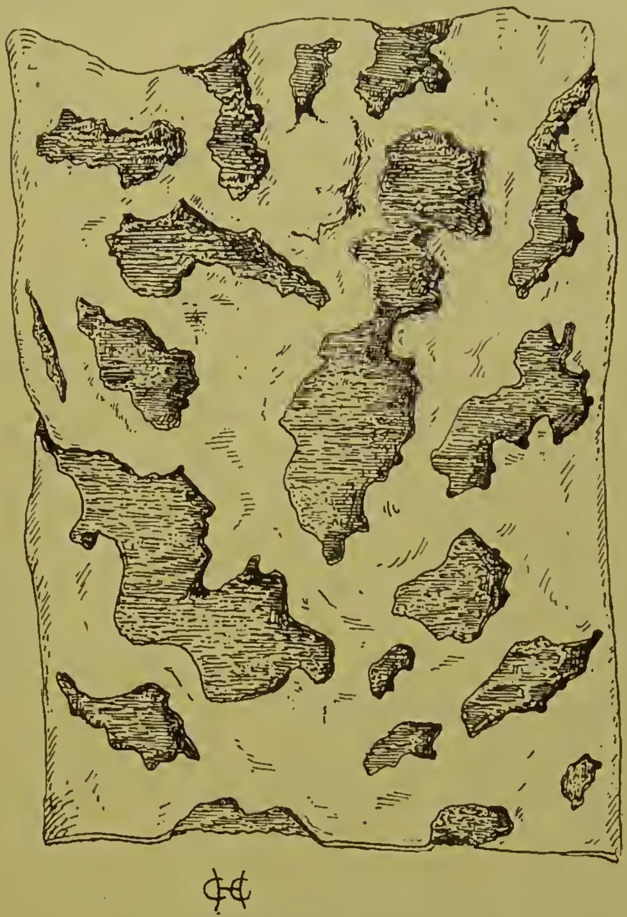


FIG. 98.—DYSENTERIC ULCERATION OF RECTUM. NATURAL SIZE.

Numerous irregular ulcers with sharp-cut edges are seen. In some places the mucous membrane is undermined. The floor of the ulcers is formed by the circular muscular coat of the gut.

(*f*) **Dysentery.**—Dysentery is essentially a tropical disease. Such cases as are met with in this country have always originated elsewhere.

The characteristic lesion of dysentery is an ulceration of the large intestine. As a rule, it is the lower part of the large gut that is affected, so that the rectum and the descending colon are most commonly found to be diseased. In severe cases, however, the ulceration is found as high as the ileo-cæcal valve, and a certain number of cases have been recorded in which there was ulceration of the lower end of the small intestine in addition.

The macroscopic picture is one of great destruction of the mucous membrane. In some instances the mucous membrane is torn into shreds similar to those which are found in ulcerative colitis. This is the case in the more severe forms of the disease, and those which run a particularly rapid course. In other cases the mucous membrane is not everywhere lost, but the ulcers leave islands of comparatively normal mucous membrane between them. These masses of mucous membrane are wider at the top than at the points of their attachment, owing to the undermining nature of the ulcerative process. As a result the still remaining portions of mucous membrane bear a somewhat fanciful resemblance to mushrooms.

Although the appearances of an intestine which has come from a case that has died during the disease have generally the features that have been described above, it is clear that these are only somewhat late changes, from the appearances met with in cases that die very early in the disease. As a matter of fact, we have to divide dysentery, like most other forms of inflammation, into an acute and a chronic variety. In the chronic variety the appearances are such as have been described, but in the acute variety the changes are those of an intensely severe inflammation into which ulceration has not, as yet, entered. For the mucous membrane of the gut is swollen and intensely hyperæmic, while its surface is covered with a mucous or grumous material which consists of desquamated epithelium mixed with blood. The entire thickness of the intestinal wall is infiltrated with exudation fluid and large numbers of migrated leucocytes. In places definite hæmorrhages are to be seen. As a result of these changes a very characteristic modification of the mucous membrane is that it is thrown into numbers of very prominent folds. It is the sloughing of portions of these folds that leads to the formation of the ulcers that characterise the chronic form of the disease.

In some cases the disease proceeds to healing of the ulcers. This takes place in the ordinary fashion with the formation of fibrous tissue. This termination of the disease is, however, a somewhat rare one. In the majority of cases the ulcers persist and give rise to a chronic muco-sanguineous discharge from the bowel. Nevertheless, even in these cases we may meet with situations in which there is evidence of cicatrisation.

The cicatrices of dysentery are usually of great superficial extent, and generally are of a very dark colour. In process of time they contract, while the more or less unaltered tissue between them becomes distended. In this way a marked pouching of the gut is produced. Quite apart from the formation of cicatrices, it is common for an intestine which has been the seat of dysentery to undergo a marked atrophy of its walls. This leads to the persistence of a diarrhœa long after the actual dysenteric diarrhœa has ceased.

With regard to the ætiology of dysentery, it is probable that there are several different varieties. In certain cases an amœba is found in the stools similar to, but not identical with, the amœba coli. In other cases the disease is of bacterial origin.

(*g*) **Fæcal ulcers.**—In cases in which there has been a long-continued accumulation of fæcal material in the colon, from whatever cause, it is common to find superficial ulcers of the mucous membrane. These ulcers differ in certain respects from the other varieties of ulceration that we have considered. In the first place, they are of the character rather of necrotic ulceration due to pressure atrophy than of that which is the result of inflammation, for they are formed at spots at which the hardened masses of fæces (scybala) have become lodged, that is, in sacculi of the colon. And, in the second place, they are unaccompanied by any evidences of inflammation. They are associated with great distension and sacculation of the gut.

(*h*) **Syphilitic ulceration.**—In the case of the large intestine syphilis is sometimes found to produce an ulcerative condition of the lower end of the rectum. In a very few cases the disease is primary, but in the vast majority it is tertiary, and the ulcer represents a gumma which has broken down.

The gummatous condition involves the submucosa, and is arranged around the entire wall of the gut, so that it leads to stenosis. In a very short time after its formation the surface of the gumma breaks down and an ulcer is formed which produces a certain amount of pus. The condition may advance until it involves the neighbouring tissues, but it is far commoner for the ulceration to be confined to the rectum. For some reason which is undetermined the condition is almost always seen in women of the poorer classes. Under treatment the ulcer may heal, and then there results a ring of dense cicatricial tissue which forms a fibrous stenosis.

While dealing with this question, it may be mentioned that fibrous stricture of the large intestine is sometimes met with which is not syphilitic. The principal seat of such stricture is the sigmoid flexure, but it may occur in the transverse or the descending colon, or even at the junction of the cæcum with the ascending colon. The condition is met with in elderly people, and is generally the result of a chronic irritation of the intestinal wall by hardened fæcal masses. It is, therefore, of inflammatory origin. In women, fibrous stricture of the sigmoid flexure is somewhat likely to occur as the result of the formation of a considerable amount of inflammatory fibrous tissue in connection with disease of the internal generative organs. Thus it may occur as the result of a severe attack of pelvic cellulitis after parturition.

(*i*) **Fistula.**—Although there are special surgical features of *fistulæ in ano*, the condition is nothing more than a sinus. It results, in the majority of cases, from the rupture of an abscess in the ischio-rectal fossa into the intestine, and the varieties of fistula depend upon the question as to whether there is only one opening of the abscess into the rectum or whether there is, in addition, an opening on the external skin. Strictly speaking, the suppurative condition which leads to the formation of a fistula should not be included amongst the diseases of the intestines, for the pus does not form in the wall of the gut itself, even at a late stage. On the contrary, the extension of the ischio-rectal abscess takes place in the areolar tissue around the lower end of the rectum, and completely loosens it from its internal attachments, but leaves the coats of the intestine practically unchanged for a long time.

(*j*) **Fissure.**—A condition of great clinical, but of little pathological importance is the occurrence of a small degree of superficial ulceration just within the anus. The ulcer or ulcers—fcr there may be two or three—are always small; they are round or oval, and very rarely exceed a threepenny piece in size. The ulceration is superficial, and the floor of the ulcer is red and gives exit to a small amount of watery exudation. The importance of the condition lies in the excessive pain by which it is accompanied. Fissure is generally associated with hæmorrhoids.

(*k*) **Tuberculous ulceration of the rectum.**—This condition is a rare one, but when it is present it is usually very extensive. We have already said that there sometimes occurs an ulceration of the large intestine in tuberculosis which is comparable with the ulceration seen in the small intestine. The present variety has certain differences. It is true that it is practically always secondary, but whereas the primary disease is usually in the lungs in the case of general ulceration of the intestine, when the ulceration is confined to the rectum the primary disease is situated in the genito-urinary tract. Thus there may be a tuberculous ulceration of the urinary bladder which perforates its walls, and, extending through the vesico-rectal areolar tissue, invades the rectum from without and ultimately leads to the formation of a recto-vesical fistula. Or, there may be extensive tuberculous disease of the vesiculæ seminales which extends to the intestine with corresponding results. In any case the tuberculous ulceration is quite localised, is generally extensive, and is accompanied by a complete destruction of the thickness of the intestinal wall. In women the upper end of the rectum may become secondarily involved in cases of tuberculous disease of the left ovary and Fallopian tube.

(4) **New-growths of the intestine.**—In the case of all varieties of new-growth—malignant as well as non-malignant—the large intestine is far more commonly affected than the small. In fact, it may be said that the small intestine as far as the upper surface of the ileo-cæcal valve and its immediate neighbourhood is practically never the seat of a tumour. This statement must not, of course, be taken as absolute, for spindle-cell sarcoma is known to occur in connection with the wall of the duodenum, for example; but it is so generally true that the exceptions may be neglected.

Only two varieties of new-growth are met with in the intestine with sufficient frequency to detain us, viz. simple adenoma and carcinoma. Other varieties of growth have been met with, but are exceedingly rare.

(*a*) **Simple adenoma** is found in the form of polypi. These polypi are of varying size, but the majority are about as large as a filbert. Their pedicle is usually somewhat thick, and their basis of attachment broad. The length of the pedicle varies; as a rule it is less than half an inch. The growth commences in the submucous coat of the intestine, and at first it is definitely intramural. As it grows, however, it projects more and more into the lumen of the gut, and at last, aided by the intestinal movements which tend to drag it from its base, it becomes definitely polypoid.

The surface of an intestinal polypus may be smooth, or the growth may be papillomatous in character. In either case the histological characters are the same. They are those of a tubular adenoma, or, if the structure be viewed from a different aspect, they are papillomata in which the mucous membrane of the intestine plays the part of the investing layer. That is to say, the centre of the tumour consists of a loose fibrous tissue which carries blood-vessels, and this is invested with a thick layer of an abnormal mucous membrane in which the tubular glands have become tortuous and irregular, ramifying deeply in the hypertrophied loose connective tissue of the submucosa, but nevertheless opening on the surface of the growth. As a consequence of this structure a section of a polypus of this kind shows, in addition to the central support of vascular connective tissue, a number of round, oval, or irregular cavities lined by a beautiful layer of columnar cells, and on the surface, a covering of columnar cells which dips into a number of crypts of varying length. Since the epithelium which covers the growth is identical with that which invests the intestinal tract generally, a certain number of the cells are of the 'goblet' variety and produce mucus. (Fig. 41.)

Although polypoid adenomata may be met with in any part of the intestine, the commonest situations are the neighbourhood of the ileo-cæcal valve, the sigmoid flexure, and the rectum. Their importance is chiefly mechanical, in that they are 'foreign bodies' in the intestine. They, therefore, may lead to one or both of two conditions. Either they cause a local inflammation of the intestine with the formation of a large amount of mucous exudation, or they lead to increased peristaltic action of the intestinal wall. In the latter case they are apt to be gripped by the contracting gut and be carried onwards, and since they are attached at their base, they drag with them the wall of the intestine itself. In this way they are often the initiating cause of an intussusception. If the constriction of the pedicle induced by intussusception or by any other means is sufficiently great, sloughing occurs and the tumour is cast off.

(*b*) **Carcinoma** of the intestine affects the large intestine in five situations—viz. in the rectum, the sigmoid flexure, the splenic flexure, the hepatic flexure, and at the junction of the cæcum with the ascending colon. The order in which the sites of carcinomatous disease have been given is approximately the same as the order of frequency with which the different parts of the gut are affected.

The new-growth is almost always in the form of an annular constriction of the intestine, and a certain amount of ulceration is always present. The degrees of stenosis and of ulceration vary considerably, and are somewhat in inverse ratio to one another. As a rule, however, stenosis is the most marked feature, and is accompanied by so great an increase in the thickness of the intestinal wall at the site of the disease that it is impossible to pass more than an ordinary pencil through the stricture, while the wall of the gut itself is frequently three-quarters of an inch in thickness. Marked ulceration of a carcinoma of the gut is chiefly seen when the sigmoid flexure is affected. In these cases the ulceration may be so considerable that the wall of the gut is entirely destroyed, and the two ends of the intestine open into a large ragged cavity which may at first give rise to the idea that it is an abscess cavity.

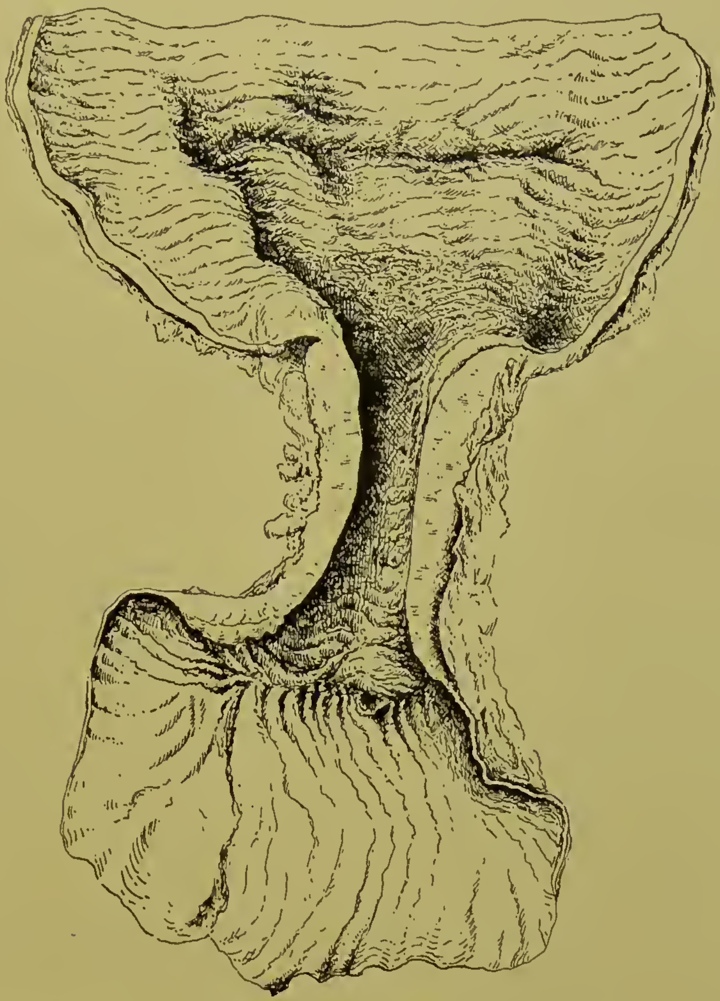


FIG. 99.—MALIGNANT STENOSIS OF COLON. × $\frac{2}{3}$.

The stenosis occurred at the hepatic flexure, and completely encircled the gut, reducing the lumen to the size of a goose quill. There is but little ulceration. The dilatation and hypertrophy of the intestinal wall above the stricture are in great contrast to the constriction and atrophy below.

The extent of the stenosed portion of gut varies considerably: in some cases the constricted portion is only about a half-inch in length, in others it is three or four inches. In almost all cases the increased thickness of the intestinal wall at the site of stenosis is largely due to a great increase in the thickness of the muscular layers. Sometimes this is so much the case that it is difficult at first sight to believe that a malignant growth is present at all.

In this respect the condition is similar to certain of the malignant stenoses of the pylorus. Above the site of stenosis the gut is always dilated, and generally the muscular coat of its walls is hypertrophied; below the stenosis the gut is atrophied and contracted.

Carcinoma of the intestine is almost always of the columnar-cell variety, but sometimes it is composed of transitional cells. So far as concerns the liability of carcinoma of the intestine to form secondary growths there is the greatest variation. Sometimes we find that the liver is saturated with nodules of growth far exceeding in bulk the primary mass of carcinoma in the intestine. But in a very large number of cases there is a complete absence of secondary growths throughout the body so far as can be discovered by careful macroscopic examination. This is a remarkable circumstance when we bear in mind the great vascularity of the intestine and the number of its absorbents. Occasionally the lumbar lymphatic glands are found infiltrated with growth, but this is much less common than to find the secondary growths in the liver.

Although it is true that in the case of the intestine proper carcinoma is of the columnar-cell variety, this is not the case when the anus is affected. For the anus is formed by an invagination of the epidermis, and therefore any cancerous growth that originates from it is of the squamous-cell type.

(5) **Abnormalities of the intestinal contents.**—It is impossible to enter into a full description of all the different characters of the intestinal contents in disease. Certain changes, however, are so definite, that they may be briefly mentioned.

When blood is poured out into the lumen of the gut the alteration in the appearance of the motions differs according to the seat of the hæmorrhage. When the blood comes from the rectum, as, for example, from the bleeding of internal piles, it is at once recognisable as blood, and it may be that definite clots are expelled. But when the blood is poured out high up in the intestine, and more particularly when it is poured out in the stomach—for example, in the case of chronic gastric ulcer—and passes thence into the intestine, it no longer has the appearance of blood, but confers to the entire intestinal contents an appearance similar to that of tar. A condition in which such tarry stools are passed is termed **melæna**. Conditions bearing a certain amount of resemblance to melæna are met with when iron and bismuth are being given as drugs. The black colour of the stools under these circumstances is due to the formation of the black sulphides of these metals.

Variation in the amount of bile contained in the fæces is also a cause of abnormal appearance of the intestinal contents. The presence of an excessive amount of bile is of little importance, but the complete absence of bile gives to the stools an appearance which has been likened, with justice, to pipeclay. When the bile is not completely absent the stools have a clay colour. The cause of this abnormally light appearance of the intestinal contents is an obstruction to the flow of bile into the intestine through the common bile duct. The cause of the obstruction may be a gallstone, or a catarrh of the mucous membrane of the bile ducts, or a complete cessation of the formation of bile. A little consideration will show that in cases of obstruction to the bile passages the obstruction must be either in the common bile duct or in the combined right and left hepatic ducts. Obstruction of the cystic duct is ineffective in this respect. Clay-coloured stools are an accompaniment of jaundice.

'Rice-water stools' are seen in cases of Asiatic cholera, and may be almost regarded as characteristic of the disease. They depend upon the rapidity with which fluid is poured out into the gut owing to the enormous extent of the inflamed mucous membrane. They are uncoloured with bile, because the inflammation involves the mucous membrane of the duodenum and consequently causes so much swelling of the mucous membrane as to obstruct the opening of the common bile duct, and because the disease is so acute that the bile-forming function of the liver is largely put in abeyance. 'Pea-soup' stools are often met with in cases of typhoid fever, and the impression a few years ago was that the condition is as characteristic of this disease as are rice-water stools of cholera. This is undoubtedly a mistake. For not only may we meet with typical pea-soup stools in diseases that are certainly not typhoid fever (e.g. lobar pneumonia), but also it is not in more than half the cases of true typhoid fever that they are observed. They depend upon a combination of insufficient absorption, excessive secretion into the intestine, shortened stay of the intestinal contents in the gut, and, perhaps, a diminished formation of bile. Any morbid condition, therefore, in which these criteria obtain may be accompanied by the presence of pea-soup stools.

To the presence of an excessive amount of mucus in stools we have already referred in connection with membranous colitis. This is, however, not the only disease in which the condition is met with. Whenever there is a somewhat chronic irritation of the mucous membrane there is an increased formation of mucus. Hence we find it in connection with such conditions as intussusception, the presence of animal parasites in the lower bowel, polypi, &c. In ulcerative colitis the intestinal contents have often a somewhat peculiar appearance owing to the characters of the inflammation itself. For the ulceration not only is an obstacle to that absorption of fluid which is the normal function of the colon, but it is also a positive cause of an increase in the amount of fluid in the gut. Hence the intestinal contents are extremely fluid. Moreover the ulcerated surface allows of a certain amount of hæmorrhage, and since the blood is not poured out sufficiently high up to become tarry, and not sufficiently low down to be clearly recognisable as blood, it possesses an appearance that is approximately intermediate, and resembles the sediment of strong beef tea. So much is this the case that it is impossible from the appearance alone to convince oneself that such a stool is not in reality strong beef tea.

A variety of stool which is highly characteristic is that which is known as the 'pipe-stem' stool. Its name is sufficiently indicative of its features. It depends upon the fact that the motion has passed through a constricted portion of gut, and therefore it is frequently seen in cases of intestinal carcinoma, though, of course, it is not characteristic of malignant disease alone. It is necessary to remember that the pipe-stem stool is only seen when the intestinal constriction is very low down in the gut. For if the constriction be present in the hepatic flexure, for example, the fæces undergo a fresh moulding after they have passed though the stenosed portion.

Enteroliths.—In the intestine we sometimes meet with solid concretions. In a large number of cases these are gallstones which have passed along the common bile duct or have ulcerated into the intestine direct, owing to adhesions between the gall-bladder and a coil of gut. In other cases the concretions are composed of phosphates of ammonium, magnesium, and calcium, together with calcium carbonate, around a nucleus of organic material such as an undigested portion of food. Intestinal concretions are far less commonly met with in man than in some of the lower animals. In cattle, for example, it is very common to find a large gastric or intestinal concretion which consists in large part of hairs which the animal has licked from its own body. In man intestinal concretions are important in that they may become lodged and lead to acute intestinal obstruction. Reference has already been made to the 'cherry-stone' bodies that are sometimes found in the vermiform appendix.

Entozoa.—Amongst the abnormalities of the intestinal contents mention must be made of the animal parasites which inhabit the gut. The actual characters of these parasites will not be described here, as they are to be found in every text-book on medicine. Only a few points will be noticed.

The animal parasites of the intestine are of three kinds, viz. amœbæ, flat worms, and round worms. The amœbæ are found in the colon principally, and are of different kinds. Some varieties may almost be said to be normal inhabitants of this portion of gut, while the amœba dysenteriæ, to which reference has been made previously, not only differs in characters from the other amœbæ, but also is a distinctly pathological inhabitant.

The Nematode, or round worms, are found in all parts of the intestine, but particularly in the small gut. They are of different kinds, and the pathological changes which they induce are different also. Thus the **Anchylostomum duodenale** lives in the duodenum, is about one-third of an inch in length, and leads to a peculiar variety of anæmia owing to the bleeding which takes place from the puncture which it makes in the mucous membrane of the duodenum. The ordinary round worm, **Ascaris lumbricoides**, is very similar to an ordinary earthworm in length and appearance. It is generally single or is present in small numbers, and it inhabits the upper portion of the small intestine principally. The 'thread worm,' **Oxyuris vermicularis**, is something less than half an inch in length and very fine. It is present in large numbers, and generally inhabits the lower end of the rectum, though it has been found much higher in the large intestine.

The Tæniada, or flat or tape worms, are far longer than those which have already been described. They frequently measure many feet from the head to the last segment. They are composed of a number of segments which are extremely small close to the head where they are formed, but increase in size lower down the organism. They are attached by the head to some portion of the mucous membrane of the small intestine, and generally only one such worm is present. The chief tapeworms met with in the human intestine are the **Tænia mediocanellata,** the **Tænia solium**, and the **Bothriocephalus latus.** Each of these has its distinctive features.

B.—THE PERITONEUM

The diseases to which the peritoneum is liable are not numerous, but they are of extreme importance in the majority of cases by reason of the great area of the serous cavity and the importance of the organs which are invested by the peritoneum.

(1) **Inflammation.**—Peritonitis is of different kinds, and the macroscopic pictures presented by these different varieties are themselves very dissimilar. We shall describe the acute without suppuration, the acute with suppuration, the tuberculous, and the chronic varieties.

(*a*) **Acute peritonitis without suppuration.**—This variety is perhaps the most acute of all the inflammations to which the body is liable. It commences at a given point, and within a few hours the entire serous membrane is intensely inflamed and the patient dies. This is, however, the case only when the inflammation is general; in many cases the inflammation is quite local, and then the ultimate condition produced is different, although the actual changes seen in the affected portion of the peritoneum during the acute stage are the same as in acute general peritonitis.

In a case which has died at an early stage of an acute general peritonitis, when the abdominal cavity is opened, the following appearances are observed. The peritoneal surface has everywhere lost its normal glistening appearance, and has become dull and lustreless. In the case of those reflexions of the membrane which cover the intestines, a series of bright red lines are visible, corresponding to the small spaces which exist at points where the coils of small intestine fail to come in contact. In these same situations a small amount of yellow slightly adherent fibrin is present, and in regions at which the spaces are larger there may be a small accumulation of slightly turbid fluid. Everywhere the peritoneum is of a rose-pink or of a definitely red colour, and at places there may be petechiæ or subserous hæmorrhages.

In a general peritonitis the appearances which have been described above are visible everywhere throughout the abdominal cavity; where the inflammation is localised the local changes in an early stage are just the same. It may be pointed out that the very closeness with which the abdominal viscera are packed is, on the one hand, an important factor in limiting a peritonitis that has commenced at one particular spot, and, on the other hand, is the chief factor in rendering it impossible to treat surgically a condition of general peritonitis owing to the number of recesses that enter into the composition of the peritoneal sac as a whole.

The histological characters of an acute peritonitis are those incident to acute inflammation generally. Hence the appearances are very similar to those which have already been described as obtaining in the case of acute pericarditis. If a section be made of the wall of a coil of small intestine over which the peritoneum is acutely inflamed, it is seen that the surface of the serous coat, instead of being smooth and covered by a single layer of endothelial cells, is ragged and rough, from the deposition in it of fibrin. At the same time it will be found that the endothelial cells covering the membrane have undergone change. They may have become entirely detached, but at the early stage of the inflammation which is under discussion this is not likely to be the case everywhere. On the contrary, we may find that the fibrin is situated over a fairly intact layer of endothelial cells, just as it frequently is when the pericardium or the pleura is acutely inflamed. In some places, too, it may appear as if there has been an actual proliferation of the endothelial cells. In the sub-endothelial portions of the peritoneum, which are normally composed of little else than a somewhat dense fibrous tissue, there are visible numbers of small but dilated blood-vessels. For the most part these are capillaries, but here and there vessels of larger calibre are present. Still deeper, one comes to the actual wall of the intestine itself, and just as in the case of pericarditis we saw that the myocardium itself suffers, so we find that the wall of the intestine beneath the inflamed peritoneum suffers. It is swollen with exuded fluid, and with numbers of migrated leucocytes, its vessels are engorged, and the muscular fibres of the middle coat have largely lost their normal appearance, and have become granular, while, at the same time, the intermuscular fibrous tissue shows the presence of an enormously increased number of leucocytes. These changes, as might be expected, are most manifest in the outer layer of the intestine.

If the condition is not sufficiently extended to lead to death, either this acute inflammation passes into a definite suppurative condition, or repair is brought about by the formation of fibrous adhesions.

(*b*) **Acute peritonitis with suppuration.**—At the very outset it must be stated that in a large number of cases of acute peritonitis without suppuration the appearances are such that it is at first supposed that suppuration has occurred. And, indeed, it is clear that cases will be met with that lie midway between the two classes. The cause of this uncertainty from the macroscopic side lies in the appearance of the fibrin which is so commonly deposited in cases of acute peritonitis. It is often quite impossible to convince oneself that the material which is present between the coils of gut is not true pus, until one has examined some of the material with the microscope. With a truly suppurative peritonitis, however, the case is, of course, quite different. For then the material scraped off the inflamed intestine is seen to be composed of little else than degenerated leucocytes, while such collections of fluid as are present in the abdominal cavity consist of typical pus.

In a suppurative peritonitis the macroscopic features of the case are dominated by the presence of a purulent fluid in the abdominal cavity which is present in far larger quantity than the small amount of turbid fluid—which is not pus—present in cases of non-suppurative peritonitis. As a rule, when the abdominal wall is divided at the autopsy, there gushes forth a moderately large amount of pure pus, which may or may not have a foul odour. This occurs in cases in which the suppurative condition is general. More commonly we find that the collection of pus is localised, although there is a general peritonitis. The localisation of pus takes place, in the majority of cases, at the point at which the inception of the peritonitis occurred.

The causes of acute peritonitis are various, and in the large majority of cases the condition depends upon some antecedent condition in one of the organs or tissues which are normally invested with peritoneum. Thus we may find that there has been a gastric ulcer which has perforated, or a typhoid ulcer which has perforated, or is on the point of perforation. Or it may be an inflammation of the gall-bladder (cholecystitis), which has either passed through the entire thickness of the wall of the gall-bladder without rupture, or has caused definite rupture and leakage of bile mixed with inflammatory material into the peritoneal cavity. Or it may be that there has been an intestinal hernia or an intussusception which has become gangrenous and has partially separated at the upper end, and has allowed a portion of the intestinal contents to escape into the peritoneal cavity. Or it may be that there has been a suppurative inflammation of the Fallopian tube or the ovary, or a retention of some material in the cavity of the uterus after parturition which has undergone putrefaction. And many other conditions might be instanced. But in all of them there has been some local condition which has involved the peritoneum, and has led to a peritonitis which was at first local. Whether the peritonitis remains local or whether it becomes general, whether it is accompanied by suppuration, or not, depends upon a number of circumstances that do not call for particular notice here.

There is one variety of general peritonitis, however, which is exquisitely suppurative. This variety is almost always found in young children of, perhaps, four to eleven years of age. It is of the acutest kind, but the most careful examination of the organs fails to discover a primary lesion from which the peritonitis might be considered to have arisen. In some cases the suppurative peritonitis is conjoined with a suppurative pleurisy, or a suppurative pericarditis, or both, but even then it is impossible to determine whether any one of these conditions was antecedent to the others, or whether their onset was independent and synchronous. There is a considerable amount of reason to believe that most of these cases are due to infection by the pneumonococcus.

In other cases of peritonitis besides that which has just been mentioned, whether suppurative or non-suppurative, it is common to be able to demonstrate the presence of micro-organisms. In many cases this may not be possible by making coverslip films alone, but only becomes manifest after cultures of the material on the surface of the inflamed peritoneum have been made. In those cases in which the peritonitis has been brought about by the rupture of stomach or intestine the micro-organisms found are of the most varied descriptions, and it is impossible to say that any particular one has had an especial share in producing the peritonitis. When the peritonitis is suppurative, however, we generally find that the number of varieties of micro-organisms present is limited, and in not a few cases we only find either streptococci or staphylococci. In most cases in which either of these two varieties is present, we have to do with streptococci, and then we may find them present in short or in long chains. Speaking very generally, it may be said that the more acute the process has been, the shorter the chains of streptococci and *vice versa*.

(*c*) **Tuberculous peritonitis.**—This variety of peritonitis is one of the most characteristic. It occurs generally in young persons below the age of puberty, but it may be met with at a little later age, and in a very few instances the condition is found in persons of middle age.

In tuberculous peritonitis we generally find that the inflammatory changes have led to so profound a series of changes in the abdomen that the viscera are recognised with difficulty. In particular the chronicity of the change is accompanied by the formation of so large an amount of fibrous tissue that the individuality of the coils of small intestine is completely lost and the incision through the abdominal wall brings us direct into some coil of gut before we have recognised that we have cut through the muscular layers of the abdomen. When we have peeled the abdominal wall from the mass of material which lies beneath, and to which it was intimately adherent, it is seen that it is impossible to trace the continuity of the gut except with the greatest difficulty, and frequently the adhesions are so numerous and the walls of the intestines themselves are so altered that no amount of trouble suffices to set them free.

In addition to the presence of a number of adhesions a tuberculous peritonitis is characterised by the presence of a multitude of small tuberculous nodules. These nodules are almost always caseous in the centre, are generally thickly disseminated throughout the abdominal cavity over the peritoneal surface, and sometimes are aggregated in large masses. At the same time such spaces as are left between the adhesions are commonly filled with a turbid fluid, but the total amount of fluid found in cases of tuberculous peritonitis is naturally small owing to the vast number of adhesions that are present.

As a rule, the tubercles are present only in the peritoneum itself, and in any case they are present in this membrane in overwhelming excess. Nevertheless we may meet with caseous foci in the spleen, for example, which are perhaps of the size of a cherry. General miliary tuberculosis of the organs, even those of the abdominal cavity, is rare. The abdominal lymphatic glands are completely altered by tuberculosis of the caseous type, but it is generally very difficult to find the mesenteric glands owing to the extent of alteration of the mesentery itself.

The condition of tuberculous peritonitis that has just been described is very different from the presence of miliary tubercles in the peritoneum in cases of generalised miliary tuberculosis. In the latter condition it is true that we frequently find minute tubercles in the capsules of the organs and in the peritoneum itself, but here the number of the tubercles themselves is far less, they are much smaller and do not show the same chronicity and tendency to caseation, and they are not accompanied by the formation of adhesions—in a word, tuberculous peritonitis is a condition *sui generis*.

Microscopically, the changes which are observed are those common to all tuberculous lesions, but we find some differences according to whether we meet with the case early or late. In any case the number of cells present is large, and in early cases the entire condition appears to be cellular throughout. In a portion of omentum, for example, we shall find in an early case that the fatty tissue has almost entirely been replaced by a cellular formation. The cells are chiefly of the endothelioid type, but round cells (presumably leucocytes) are present in great numbers. Probably a certain number of giant cells will be found, but it is quite possible that it will be necessary to search through a good many sections before their existence is demonstrated.

One of the situations in which the actual nature of the process may be best examined is the under surface of the diaphragm. The reason of this is that here the tubercles, although numerous, are commonly not so thickly studded that the underlying material is entirely obscured. Moreover, the adhesions between the diaphragm and the upper surface of the liver are generally fairly soft and broken down with ease.

(*d*) **Chronic peritonitis.**—Strictly speaking, by the term ‘chronic peritonitis’ should be meant a chronic inflammatory condition analogous to that which occurs in other organs. But in the case of the peritoneum we meet with the same difficulty which has presented itself elsewhere, in that conditions are included under the name which are not clearly dependent upon inflammation at all. Thus the peritoneum is sometimes found to be locally or generally thickened, and this is assumed to be a late result of an antecedent inflammation. It must be conceded, however, that in the case of this membrane the probabilities that the condition is fundamentally dependent upon an inflammation are greater than they are in the case of many other tissues.

The commonest conditions under which we meet with chronic peritonitis are those which are associated with ascites. Thus it may occur in chronic heart disease, and generally in any condition in which there is an obstacle to the flow of the blood through the portal vessels because of an alteration in the consistency of the liver. Under these circumstances we may meet with either a local or a general chronic peritonitis.

Chronic peritonitis is characterised by a thickening of the peritoneum itself and a replacement of the semi-translucency of the membrane by a less or greater degree of semi-opacity. In a well-marked case the membrane has a smooth, shining, opalescent appearance, and though there are no marked irregularities on the surface, it is evident that the thickness of the membrane is not everywhere the same. In places there may be a certain amount of loosely attached fibrin which has separated from the ascitic fluid, and when the condition has definitely originated from an antecedent inflammation of a certain degree of acuteness, fibrous adhesions may be present also. It is very rare, however, for adhesions to form a great feature of the peritoneal change. Such a condition may be fairly evenly distributed over the entire extent of the peritoneum.

In cases of very long duration, and particularly in those which have been frequently tapped in order to remove the accumulated ascitic fluid, the amount of fibrin present is considerable. In these cases it may be so deposited as to form a very definite false membrane and to present a misleading appearance. Thus in cases of chronic ascites due to alcoholic cirrhosis of the liver, it is common to find that the intestines have been drawn up into a ball owing to the shortening of the mesentery consequent upon chronic peritonitis, and then covered over by a thick layer of fibrin. As a result of this change the intestines seem to lie in a bag, and at the first glance it may be difficult to see where they are situated. For, instead of filling the abdominal cavity and the pelvis, they are gathered together at the back of the abdominal cavity close to the vertebral column, and the pelvis and the main portion of the peritoneal cavity seem to be converted into a mere cyst which contains nothing else than ascitic fluid. A similar change to that which affects the mesentery also affects the omentum, so that it, too, may become rolled up into a thickened mass which lies at the upper part of the abdominal cavity, is scarcely recognisable as omentum, and is a source of immense difficulties in the way of diagnosis clinically. (Fig. 16.)

Not infrequently we meet with a localised condition of the capsules of organs normally covered with peritoneum that is completely analogous to the 'corns' which have already been described as occurring on the surface of the heart. The condition consists in the formation of a mass of dense fibrous tissue which has a lamellar arrangement. From the latter circumstance the formations are sometimes called 'lamellar fibromata.' The commonest situations in which they are found are the spleen and the liver. In the case of these organs the capsule may become completely and fairly evenly converted into a mass of dense white fibrous tissue perhaps an eighth of an inch in thickness, but more commonly the thickening takes place irregularly, so that there are numbers of foci of different sizes which more or less completely cover the entire organ. This particular change is generally accompanied by the presence of firm fibrous adhesions between the capsule of the organ and surrounding tissues. A condition of this kind may or may not coincide with an accumulation of ascitic fluid in the abdominal cavity, but under any circumstances it is only liable to be found under conditions in which it is common to have ascites.

(2) **New-growths.**—Primary new-growths of the peritoneum are very rare, and even in the case of those new-growths which affect the peritoneum, and which we are disposed to look upon as primary, there is always the possibility that a small growth was present in one of the tissues that are covered by peritoneum, and was really primary but overlooked.

The most important primary new-growths are **endotheliomata**; they manifest themselves as smooth multiple excrescences on the surface of the serous membrane, which may be isolated or may run into one another. Sometimes they form solitary tumours, but this is less common than the production of strands which pass from one point of the peritoneal surface to another, and are broken by the presence of small white elevations.

The tumours are generally of soft consistency and colourless. Histologically, they consist of a somewhat firm connective tissue in the meshwork of which are accumulations of cells in the form either of alveoli or of strings. The condition is generally accompanied by the presence of a certain amount of serous or sero-fibrinous fluid in which blood is mixed.

Secondary new-growths of the peritoneum are fairly common, but in the majority of cases we find only a limited number of nodules present. In some cases, however, the greater part of the whole peritoneal cavity is filled with growths which spring from the membrane. Under these circumstances we generally have to do with a growth which has started in the intestine or the ovary, and in addition to the presence of enormous numbers of nodules we are liable to find that the carcinomatous cells have undergone a colloid degeneration. In the case of ovarian growths the variety which is most liable to be accompanied by the formation of secondary nodules in the peritoneum is the papilliferous cystadenoma. When the cyst has ruptured, the masses of epithelium which are set free attach themselves to the peritoneum and there continue to grow. Under these circumstances the masses may preserve their papillomatous characters or they may form definite nodules with fairly smooth and regular outlines. The under surface of the diaphragm is a very favourite situation for such secondary nodules, and sometimes the general appearances are at the first glance highly suggestive of tuberculosis.

Other morbid conditions of the peritoneum, such as the presence of hydatid tumours, secondary nodules of sarcoma, &c., are known to occur, but they are so rare that they need not detain us.

SECTION X

THE LIVER AND BILE PASSAGES

OWING to the large size of the liver and the important position in which it stands with regard to the entire alimentary tract, the number of morbid conditions which affect it and the bile passages is considerable. In the majority of cases, too, the hepatic changes are not isolated, but are accompanied by other changes in the body, whether they are the causes, or the results, or merely the accompaniments of those changes.

A.—THE LIVER

(1) **Vascular changes other than inflammatory.**—The principal modification of the vascular supply of the liver consists in chronic venous congestion. This condition is due to any cause which impedes the passage of the blood in the vena cava inferior or in the heart,. and therefore is most commonly met with in chronic cardiac disease.

(*a*) **Chronic venous congestion.**—The alteration which is produced in the liver under these circumstances is very characteristic. The liver itself is enlarged and hard, its capsule is smooth and its edge more rounded than normal. Its colour varies from a deep purple, which occurs when the condition of venous congestion has not been of long duration, to a mottled colour, in which red, yellow, white, and brown are to be recognised in varying proportions in different places. The latter appearances are characteristic of a long-continued venous congestion, and have caused the organ under these conditions to be called the *nutmeg* liver, from its appearance on section to the section of that fruit.

The actual appearances of a section of a nutmeg liver depend upon the presence of foci of which the principal constituents differ. Thus those foci which are red owe their colour to the fact that at these spots the capillaries are fuller of blood than elsewhere; those which are white to the presence of a considerable amount of fat; those which are brown to a considerable accumulation of pigment in the hepatic cells. The yellow spots are generally of a very bright colour, and owe their existence to the staining of the tissues with bile.

The histological features of a nutmeg liver are very characteristic. In a condition which essentially depends upon an increase in the intravenous pressure throughout the liver, and which is associated particularly with an obstruction of the flow in the inferior cava, it is clear that the part of the lobule which will chiefly suffer must be the centre of the lobule. Hence we find that the central vein is widely distended with blood, and that the capillaries throughout the lobule, but more particularly those in the immediate neighbourhood of the central vein, are dilated and engorged. These changes cannot take place without exerting an abnormal pressure on the hepatic cells in the centre of the lobule,

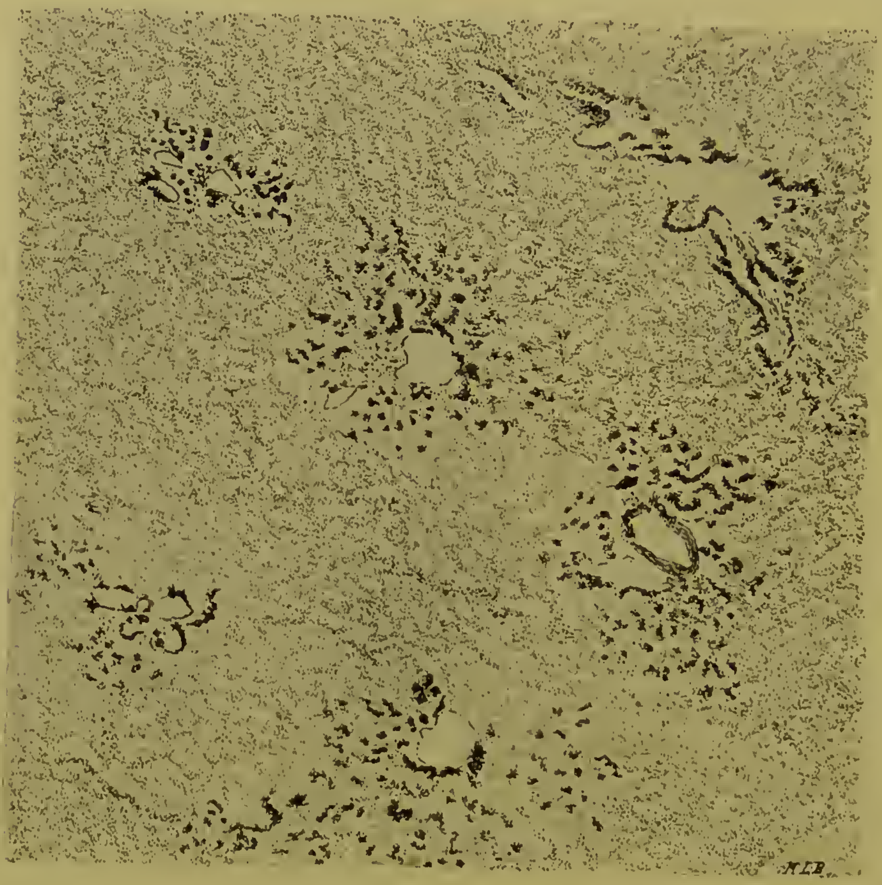


FIG. 100.—'NUTMEG' LIVER (CHRONIC VENOUS CONGESTION.) × 60.
The pigment is arranged chiefly around the intralobular and sublobular veins. The former chronic congestion is shown by the innumerable clear, irregular, interlacing spaces in the liver substance itself, which a higher magnification shows to be dilated capillaries.

and therefore in conjunction with the congestion we find a variable, but generally considerable, degree of pressure atrophy of the liver cells, which in its turn is most manifest in the centre of the lobule. The red foci in a nutmeg liver are therefore situated chiefly in the centres of the lobules.

The congestion which is present throughout the liver is not without its effect upon the red blood corpuscles themselves. Many of them disintegrate, and the pigment which is formed as the result of their destruction is stored up, in large part, in the hepatic cells closest to the seat of its formation. That is to say, the hepatic cells closest to the central vein are liable to show the presence in them of granules of yellow or brown hæmatogenous pigment. These same cells are moreover undergoing a fatty degeneration in the course of their atrophy from pressure, and hence around the red central focus there is a somewhat irregularly disposed zone which is more pronouncedly white or brown according as more fat or more pigment enters into its composition.

The bright canary-yellow foci or lines that are visible in a nutmeg liver are situated in the periphery of the lobule. Microscopically we may find that the bile pigment has stained only the lining epithelium of the bile ducts themselves, or that the colour has diffused through the entire wall of the bile duct and has passed into, and stained, the peripheral hepatic cells of the lobule.

The changes which have been described are those which are characteristic of chronic venous congestion of the liver, but they are not the only ones that are found in a case that has been of some duration. For it is a characteristic of tissues that are the seat of a long-continued venous congestion that they undergo a proliferation of the connective tissue that enters into their composition. The liver is no exception to this rule, and therefore we find in a certain number of cases that there is a general increase in the amount of fibrous tissue throughout the organ. In many instances, no doubt, there is an uncertainty whether this additional fibrous tissue may not have been present before the chronic venous congestion occurred, being, therefore, due to some other cause. But nevertheless a considerable number of cases remains in which this possibility is excluded. Such, for example, are cases of chronic mitral disease in young children.

(*b*) **Infarction.**—Infarcts of the liver are very rare compared with their occurrence in other organs, and the conditions which apparently underlie their formation seem to be different. The commonest cause of infarction of the kidney and the spleen is undoubtedly chronic or acute heart disease, but it may almost be said that heart disease is never the cause of infarction of the liver. On the other hand, we find hepatic infarction associated most commonly either with malignant disease of the organ, or with severe injuries, or with pylephlebitis.

Infarcts of the liver may be of the red or of the white variety, and both kinds may coexist at one and the same time in the organ. Of the two varieties, the red are the commoner, and are usually the smaller; anæmic infarcts of the liver are hardly ever found except of considerable size. The shape of a cone, or, on section, of a wedge, that is characteristic of infarctions in other organs, is not found in so typical a degree in the case of the liver. On the contrary, the larger number of hepatic infarcts are more or less regularly quadrangular on section. They are generally found with their bases at the surface, but infarcts are sometimes seen in the very substance of the liver.

Microscopically, hepatic infarctions show no very characteristic features. In the hæmorrhagic variety the capillaries are filled with blood, and a certain amount of blood has passed beyond the limits of the blood-vessels and has encroached upon the hepatic cells themselves. Such extravasation is never great, however, owing to the density of the hepatic substance itself, and for this reason, among others, a hæmorrhagic infarct of the liver is of a dull purple rather than of a deep red colour. At the same time the liver cells show evidences of degeneration. Their protoplasm becomes granular, their nuclei stain badly and tend to break up, and fat globules make their appearance. The features of an anæmic infarct of the liver are similar, excepting that the blood changes are completely wanting elsewhere than at the margins. In addition to the degenerative changes in the cells themselves, similar to those which are present in the hæmorrhagic variety also, evidences may be found that the process has been one of coagulative necrosis in the existence of a few strands of fibrin scattered throughout the necrosed mass.

(2) **Degenerations and infiltrations.**—When the liver is the seat of a degenerative or an infiltrative change, it is usual for the alteration to be manifested throughout the entire organ. Sometimes, it is true, we meet with a more or less localised change when the metamorphosis is fatty, but even in this case it is not that the change in question is absent from the rest of the organ, but that it is present in a more marked degree at the particular points at which it is recognisable with the naked eye. The change that occurs in typhoid fever and in a few other conditions (focal necrosis) is also localised, but here the alteration

is more profound, and the cause of its appearance is a definitely local one.

(*a*) **The lardaceous change** frequently affects the liver under those conditions in which the change is liable to show itself. In the liver the brunt seems to be borne by the capillaries between the individual liver cells, but it is very probable from the appearances that the hepatic cells themselves are also affected. The larger blood-vessels (arterioles and venules, both hepatic and portal) are liable to show the change in their middle coats as in other tissues of the body. The degree to which the change is visible varies considerably in different cases. In one it may be quite slight, in another it may affect the entire lobule and practically the entire liver. Under any circumstances the change first appears, and is ultimately most marked in the middle zone of the lobule.

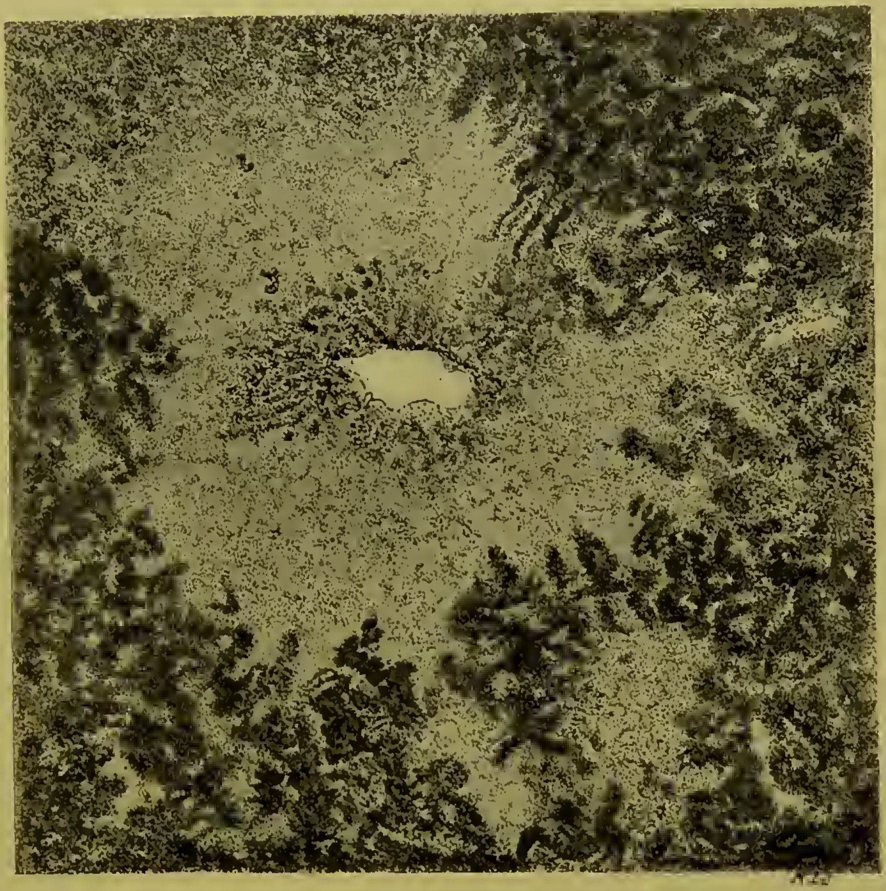


Fig. 101.—Lardaceous Liver. × 80.

A lobule of the liver showing advanced lardaceous change. The change occupies the middle zone of the lobule. The section has been very deeply stained with hæmatoxylin to show the difference between the normal (dark) tissue and the lardaceous material which stains only slightly. The lardaceous material is present in more or less rounded homogeneous masses between which the nuclei of a few remaining hepatic cells are visible.

The usual explanation of this distribution is that the middle zone of the lobule is that which is the especial region of the capillaries terminating the branches of the hepatic artery. The hepatic cells themselves undergo pressure atrophy.

The liver which is affected to any considerable extent by lardaceous disease is much enlarged, its edge is rounded, its consistency is greatly increased, so that the organ feels tough, and it has a peculiar semi-translucency on section. If a very thin slice of the organ is held up to the light, the situation of the lardaceous material is easily determined by the greater translucency, and then it is seen that the masses are circular or oval or irregular (but with rounded angles), and that there is a narrow line of opaque tissue between two adjacent masses of the lardaceous material. This appearance of a thin slice is not seen in the case of any other change.

(*b*) **The fatty change** may show itself either as a somewhat localised alteration of the liver or as a general change. The local form generally occurs in the shape of small patches of a light yellow material situated immediately beneath the capsule of the organ. This condition is so commonly seen as to be almost physiological, and certainly, so far as is known, it is without pathological significance. It is very often met with in the livers of young children. Histologically, the only observable change is that in the altered region the liver cells contain a larger amount of fat than normal, which is present also in larger droplets than normal.

The fatty changes that occur in the liver, more strictly speaking, are of two kinds, so far as the actual change is concerned. Either a true infiltration may be present or a true degeneration. More commonly when the change is a degeneration, this is combined with a certain amount of infiltration. The difficulties in deciding which of these two forms of fatty change is present have already been insisted upon, but in the rare instances in which the question is beyond doubt (i.e. conditions in which we meet with the change at its very commencement) we find that there is a difference between the portions of the lobule that are affected in the two cases. In a case of very early fatty infiltration of the liver, the fat globules are arranged around the lobule in the very periphery—that is, in the region of the branches of the portal vein by which it is assumed that the fat is carried to the liver. In an early case of fatty degeneration, on the other hand, such as that which results from poisoning by phosphorus, arsenic, or antimony, the fatty change is seen to affect the entire lobule.

It is generally said that one difference between fatty infiltration and fatty degeneration lies in the difference in the sizes of the fat droplets in the two cases. No doubt it is true that in most cases of fatty degeneration the droplets are smaller than they are when the change is infiltrative, but it is equally true that in the early stage of fatty infiltration the droplets are extremely small and regular in size, and that in a late stage of fatty degeneration the droplets are often large and of variable size.

The occurrence of fatty changes in the liver constitutes the commonest of all pathological changes. Indeed, it is impossible to declare, in many instances, that they are not physiological. They are seen in almost all cases in which the patient has long been confined to bed before death, especially if the disease has been accompanied by a small amount of fever; they occur in all diseases that are accompanied by the production of a profound anæmia, in many cases of chronic, and in some cases of acute, poisoning, in chronic alcoholism, and secondarily in the case of disease of practically any organ of the body. Hence it comes about that in many diseases in which the tissues generally are stripped of the last traces of fat, we find that the liver differs from all in being intensely fatty. A notable example of this statement occurs in the case of pulmonary tuberculosis.

A fatty liver is generally enlarged, and its edge is rounded. Its aspect is pale or yellowish, and on section the surface has a greasy look. In very advanced cases droplets of fat may be seen on the surface of the knife that was used to make the section. Owing to the amount of fat present, the consistency of the organ is diminished, and it readily breaks under the pressure of the finger. The total amount of true liver substance present is diminished proportionately to the amount of fat. This can be easily seen in specimens which have been kept in alcohol, and particularly those which have passed through the stages necessary for embedding in paraffin. In sections prepared after this manner, the former situations of the fat drops are marked by a number of circular lacunæ, and the amount of true liver substance that is left is often surprisingly small.

(*c*) **Siderosis** is a condition in which iron is deposited in the cells of an organ. It is principally seen in the case of the liver, and the disease in which it occurs to the most marked extent is pernicious anæmia. It is often spoken of as 'Quincke's siderosis,' after the pathologist who first drew attention to the change. The deposition of iron takes place in the hepatic cells of the middle and outer zones of the lobule, and the deposition is so regular that when a microscopic section has been appropriately treated, the position of the iron forms a delicate tracery over the section that can readily be observed by holding the specimen up to the light. At the first glance the suggestion given by the section is that the iron is deposited in the periphery of the lobules, but more careful examination shows that this is not entirely the case. (Plate II, A.)

The fact that a liver is the seat of siderosis is often to be recognised at the autopsy by the black colour of the under surface of the liver where it comes into contact with the colon. The change is, of course, due to the formation of the sulphide of iron.

(*d*) **Vacuolation.**—A change in the liver cells which is probably degenerative, but concerning which we have only slight knowledge, is the existence of vacuolation. The change, indeed, is not confined to the liver, although it is more commonly seen in this organ than elsewhere. The vacuoles are of various sizes, but in some cases almost reach to the limits of the cell and push the nucleus on one side. More commonly two or three vacuoles are present, and then the nucleus is, as it were, suspended in the centre of the cell. The vacuoles themselves are filled with a colourless fluid, and the change is one which accompanies the more severe degenerations and affections of the liver. The change is not an uncommon one.

(*e*) **Focal necrosis.**—In several of the acute infective diseases there is a tendency for portions of the hepatic tissue to undergo a definite necrosis. This is particularly the case in typhoid fever. The foci of necrosis are generally situated around small branches of the portal vein, and the destruction of the tissue is so complete that nothing is visible more than a granular *débris* which stains badly, and gives only the slightest evidence that it was formerly composed of cells. The foci are commonly rounded in shape, and there is a very considerable regularity in their size. As the result of the degeneration the foci are somewhat softened, but there is no formation of small softened spots in the liver which could lead it to be supposed from the macroscopic appearances that the organ was the subject of focal necroses. The foci are sometimes the seat of accumulations of bacteria.

Although typhoid fever is the commonest condition in which these focal necroses are seen, their existence is not confined to that disease. They have been met with in ulcerative colitis, in eclampsia, and it is probable that they exist in a large number of acute infections of the intestinal tract.

(*f*) **Acute yellow atrophy.**—This disease is one of the most formidable to which the liver is liable. Fortunately it is a rare disease, but the rapidity with which it runs its course, the enormous destruction which occurs in the liver, and the impossibility of arresting the degenerative changes combine to make the disease justly feared.

Macroscopically, the condition of the liver is one of intense disorganisation. The organ is much smaller than normal, weighing, perhaps, two pounds instead of over three, is extremely flabby, and shows on section that it is composed of two kinds of material, the one of which is red, the other yellow. The diminution in size takes place very rapidly; in fact, by percussion during the patient's lifetime it is possible to trace the diminution in size quite easily until a time comes at which the liver dulness is no longer given. The gall-bladder is generally empty, but it may contain a small amount of pale bile-stained fluid.

The histological changes are of so profound a kind that it is difficult to believe that the section under the microscope consists of hepatic tissue at all. The appearances differ somewhat in the yellow and in the red patches. In the yellow patches the hepatic disorganisation is complete. The cells are broken up into *débris* which hardly stains at all or shows the presence of tingible elements. A small number of leucocytes may be present, and these stain more or less normally, but this is all. At the same time there is present in these patches a considerable increase in the amount of fat, but the globules no longer are contained within cells, but lie free. In the red portions, although to the naked eye they appear to be the more profoundly altered, the changes are not so advanced. Although the modification of the liver substance is very great, the fact that one is looking at liver substance is still recognisable. But the cells have become granular, in many places they have broken down altogether, and the presence of numbers of red blood corpuscles both indicates the fact that hæmorrhages have occurred and explains the red colour of the patches. In these red patches we do not find the same large number of free fat globules as in the yellow, nevertheless some are sure to be present. In addition to the changes which have been described, bacteria of different sorts will be found in both varieties of degenerated material; but it is impossible to say how far they are concerned in the production of the process, how far they are subsequent and, so to speak, accidental invasions of the degenerated hepatic material from the intestine.

If the disease has been some weeks in existence, and has run a somewhat more chronic courset han is normal, we may find in the less altered portions of the liver that there has occurred a proliferation of the connective-tissue elements of the organ with the production of a definite amount of new fibrous tissue. In the midst of this newly formed fibrous tissue are numbers of cells arranged in strands which bear a close resemblance to those conditions which in certain other diseases of the liver are supposed to represent a new formation of bile ducts. Such a condition is not likely to be found unless the disease has lasted at least four weeks, or about double its usual length.

It is a question whether we ought not to include acute yellow atrophy amongst the true inflammations of the liver. It is in the highest degree probable that the disease is infective in the sense that it depends upon the action of micro-organisms and their toxins, and from this point of view it is certainly inflammatory. Nor does the fact that degenerative processes are so much in the ascendant modify the question, for we already know that the character of an inflammation differs greatly in different cases, and that when the tissue affected is highly cellular and the irritant is of great intensity, the necrotic portions of the process are apt to be overwhelming. The same arguments are applicable in the case of focal necroses.

A condition very similar to that obtaining in acute progressive atrophy is seen in cases of acute phosphorus poisoning. In chronic phosphorus poisoning we meet with a pronounced fatty degeneration of the liver of a more or less ordinary type, but when the poisoning is acute it is impossible to determine from the appearances of the liver alone whether phosphorus poisoning or acute yellow atrophy has led to the patient's death.

(*g*) **Leuchæmia.**—A condition affecting the liver which may be mentioned here, although it hardly comes into the category of an infiltration or a degeneration, is that which occurs in leuchæmia. In this disease there is generally found a considerable increase in the number of leucocytes that exist in the liver. The increase takes place principally in the neighbourhood of the portal venules, so that the acini appear to be surrounded by a zone of greyish material. At the same time the general increase in the number of leucocytes throughout the organ causes it to be much paler than normal. Sometimes definite masses of cells are present, and form macroscopic tumours similar to those which occur in lymphadenoma.

Microscopically, the leucocytes are seen to be chiefly aggregated in the connective tissue at the periphery of the lobule, but numbers are also present in the capillaries between the individual liver cells, and in any blood-vessel that may be seen in cross section they are sure to be present, as elsewhere in the circulation, in greatly increased numbers. Special staining will sometimes show that the great number of leucocytes present are of the oxyphil granular type; in other cases they appear to be lymphocytes.

(3) **Inflammatory affections.**—Truly inflammatory affections of the liver are not of very common occurrence. They are practically confined to the conditions of acute hepatitis and the various changes in the organ which are accompanied by suppuration.

(*a*) **Acute hepatitis.**—Acute hepatitis is an uncommon condition, if we are to judge by the comparative rarity with which we meet with those histological alterations in the liver that, elsewhere, we regard as inflammatory. Nevertheless, we meet occasionally with cases in which the connective tissue of the organ is the seat of a marked small cell infiltration. Mostly, the condition is seen in company with a general increase of fibrous tissue such as occurs in the chronic fibroses of the liver. Macroscopically, there is generally nothing to indicate that the organ is the seat of inflammation.

The condition differs in many respects from the inflammation which occurs in other tissues. It is unaccompanied by congestion, so far as can be seen, and swelling is absent. So far as pain is concerned, there may be none at all, or there may be a dull aching pain in the hypochondrium.

(*b*) **Suppurative conditions.**—When suppuration occurs in the liver, it may show itself in several ways. Either there may be formed one, or perhaps two or three large abscesses, or there may be a general suppurative condition of the connective tissue in the immediate neighbourhood of the portal canals, with the local formation of abscesses of large size, or there may be a formation of numerous small abscesses throughout the liver substance generally, or there may be a localised suppuration induced by some foreign body which acts as a local irritant. Under each of these different circumstances the macroscopic appearances of the case are peculiar, although the histological changes and the process at work which bring them about are, in all cases, the same.

(*a*) **Tropical abscess.**—The conditions under which we meet with one or at most two or three large abscesses in the liver are those which constitute the disease known as *tropical* abscess, from the fact that they are more commonly seen in persons who have lived in the tropics. As a matter of fact, they bear a very close relationship with dysentery, and it is highly probable that dysentery is their direct precursor. This is the more probable in that the amœba dysenteriæ, which is present in the intestine in some forms of dysentery, has also been found in the pus obtained from some of the tropical abscesses.

The abscess cavity in these cases is generally large; in some cases it contains a pint or more of pus. It is liable to be situated in the right lobe of the organ towards the back. The wall of the cavity is fairly smooth and consists of a thick layer of creamy material which is intimately connected on its outer surface with the liver substance, and from which portions may sometimes be stripped and constitute a sort of membrane. The abscess points in the direction of least resistance and may rupture in various directions. Thus it may perforate the diaphragm after the formation of adhesions between the liver and the diaphragm and rupture into the pleural cavity, or it may rupture into the pericardium or the peritoneal cavity, or, in fortunate cases, it may contract adhesions to the transverse colon and rupture into it. These are the commonest directions in which the tropical abscess is liable to rupture, but in many cases the patient dies before rupture takes place, from exhaustion, or the abscess is opened surgically.

(β) **Pylephlebitis.**—In this condition there is a more or less diffuse suppuration in the liver confined to the portal vessels and their neighbourhood. It commences by phlebitis with thrombosis of the portal vessels, which is induced by the lodgment of some infective material from the intestinal area. Once the inflammation has commenced, it advances by continuity of thrombosis and of the vessel-walls and the connective tissue in which they lie, until the whole or the greater part of the portal system is affected. The disease does not generally lead to any marked changes of the surface of the organ, but when an incision is made into it, it is at once seen that the tissue is intersected in all directions by dilated pus-containing cavities which at certain points form definite abscesses with very ragged outlines and walls. As a rule the pus in the cavities is creamy and yellow, but sometimes it is grumous from the admixture of broken-down blood clot.

In a great majority of cases the cause of the pylephlebitis is evident at the autopsy, or at least there has been existent at some previous time a condition to which it may fairly be ascribed.

Generally it depends upon an inflammatory condition of the intestines, and perhaps the commonest seat for the primary disease is the appendix. It is not in all cases, however, that we are able to specify the cause upon which the hepatic condition depends, and then it is sometimes spoken of as idiopathic, although our modern conceptions forbid us to believe that the condition actually arose in the liver spontaneously. It is, of course,

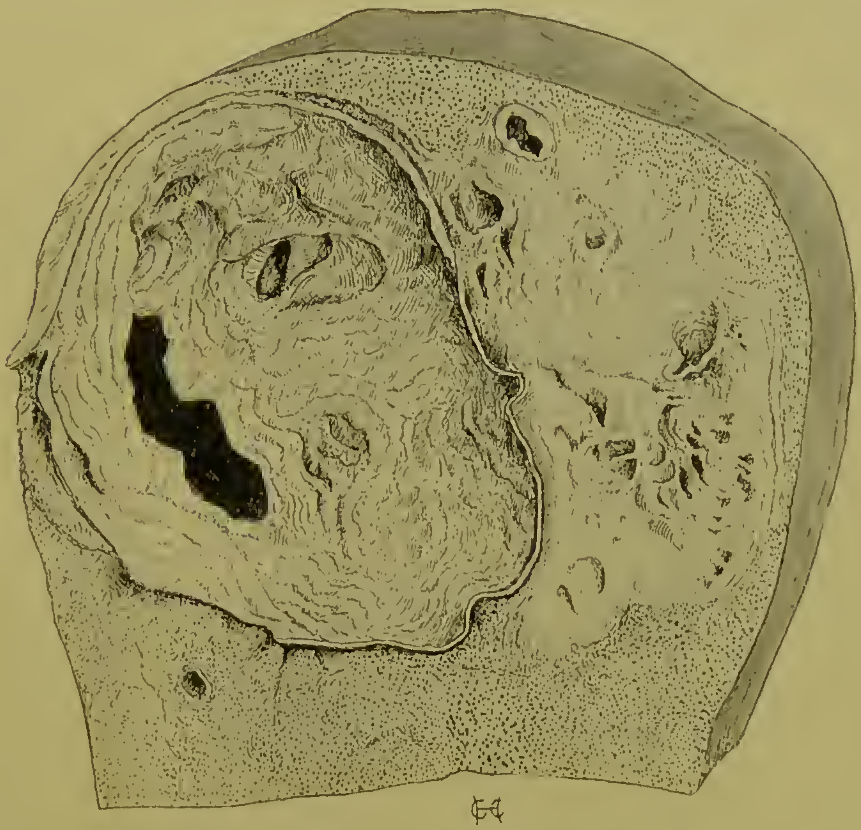


Fig. 102.—Pylephlebitic Abscess of the Liver. × $\frac{3}{4}$.

To the left is a large abscess cavity cut across which communicated with another large abscess behind (the opening only is seen). The walls of the abscess are firm and rugose, and there is a well-marked 'pyogenic membrane.' To the right is a collection of smaller abscess cavities situated in or having originated in branches of the portal vein. There is much necrosis of liver substance around these small abscesses, and ultimately they would have coalesced into a single large abscess.

possible that the intestinal condition was trifling, or that the hepatic lesion originated from an absorption of morbid material which failed to give rise to any change in the intestine. There is ample evidence that pathogenetic material may infect the liver from the intestine by travelling up the bile ducts.

In pylephlebitis the suppurative condition rarely extends beyond the liver. The reason of this is, that the process in the liver itself is so extensive that it destroys life before time has been given for it to invade other tissues by direct extension. Sometimes, however, we find that large branches of the hepatic vein have become involved, and then the process may become generalised by way of the circulation. This does not make any great difference in the severity of the symptoms, however.

(γ) **Pyæmic abscesses.**—The liver is sometimes the seat of abscesses that are frankly pyæmic. In these cases, and they are rare, the suppurative condition in the liver offers no differences from the suppuration that occurs in joints and in the subcutaneous tissues in pyæmia. For the most part the abscesses are of minute size, but sometimes they are fairly large. Under no circumstances do they reach to the size of the abscesses that we see in tropical abscess or in advanced cases of pylephlebitis. Nevertheless in pylephlebitis the abscesses vary so considerably in size that we may meet with large pyæmic abscesses that are as large as small pylephlebitic abscesses.

(δ) **Suppuration around a foreign body.**—Suppuration in the liver induced by the presence of a foreign substance may be met with under numerous conditions, but the commonest is when a hydatid cyst suppurates. In this case the suppuration commences around the cyst at the expense of the liver substance. But it involves the hydatid cyst secondarily, so that when it is opened the fluid that escapes is turbid and it may be creamy. The pus is, of course, mixed with the ordinary contents of a hydatid cyst, but the parasites are all dead. In fortunate cases, after suppuration has occurred, the process recedes, and then the fluid portions of the pus are absorbed, with the ultimate production of an encapsuled putty-like mass. In this mass portions of degenerated hydatid cyst wall are visible and hooklets may be found; these afford sufficient information as to the nature of the mass. The capsule of the mass itself is often calcareous.

A suppurating hydatid cyst need not however become converted into an innocuous mass. It is perhaps more likely to behave just like any other abscess and point in some direction or other. The directions which it may take are much those which are taken by a tropical abscess, only that the variations in the case of a suppurating hydatid are somewhat greater owing to the fact that there is not quite the same tendency for a hydatid cyst to be present in the right lobe of the liver as there is for a tropical abscess.

(c) **Specific Inflammations.**—We now turn to the more special forms of inflammation of the liver and have to consider syphilis, tuberculosis, and actinomycosis.

(*a*) **Syphilis.**—The liver is one of the organs upon which syphilis exerts a great influence. It suffers both in the acquired and in the inherited form of the disease. Changes that are met with in the acquired form consist in the formation of gummata; in the congenital disease we may find gummata present, but far more commonly we meet with a special variety of fibrosis of the organ. The gummatous change we shall consider here, but it will be convenient to defer a description of the fibrotic change until we come to deal with the fibrotic changes affecting the liver in general.

Although it is usually clear when we meet with a case of gumma of the liver what the condition is, and although we are able in many instances to state definitely that a given liver has formerly been the seat of gummata, it is not very common, at least in London, to meet with gummata of the liver. In spite of the great prevalence of syphilis, it is not in more than about one per cent. of autopsies that the liver shows well-marked gummata or signs of their previous existence.

In a gummatous liver two facts are striking; the first is the presence of a larger or smaller number of foci of cheesy material, and the other is the presence of a large amount of semi-translucent, grey, or pinkish, newly formed fibrous tissue which surrounds the cheesy masses and spreads from them, as centres, throughout the organ, and reaches up to the capsule in many places. A section of a gummatous liver has, therefore, a perfectly characteristic appearance (fig. 24).

In an early stage of the condition the amount of fibrous tissue that is present is small, and the amount of cheesy material is large. Still earlier there can be no doubt that the syphilitic disease shows itself by the presence of a newly formed material of the granulomatous type, but we do not find evidences of this condition except in rare instances and at the margins of the gummatous patches. In a well-defined case the microscope reveals nothing more than the cheesy substance and a fibrous tissue which is for the most part dense and contains few cells, but may, in places, be cellular, and give appearances usually ascribed to the formation of new bile ducts. At this time the fibrous tissue has not begun to contract to any great extent.

At a later stage the appearances are altered by the fact that the connective tissue contracts, and the older the condition, the greater the contraction. As a result of the presence of large tracts of fibrous tissue in the centre of the liver which reach up to the surface, the surface of the organ becomes puckered, and definite cicatrices are visible. At the same time the amount of cheesy material undergoes diminution, probably as the result of its compression, until at last it may disappear entirely, and then we have the production of a liver which shows one or more deeply depressed and puckered cicatrices. Such a condition of the liver is as characteristic of antecedent syphilis as is the existence of gummata themselves.

There is no particular distribution of gummata in the liver, and hence the symptoms of the condition may vary from nothing at all to a condition of intense jaundice produced by pressure on the common bile duct, or ascites, due to pressure on the portal vein. In almost all cases the condition is unaccompanied by pain.

(β) **Tuberculosis** of the liver is a decidedly rare condition if we except the cases in which it is affected, along with the other tissues and organs, in a case of generalised miliary tuberculosis. In very rare instances tuberculosis occurs in the liver in the form of caseous nodules similar to those which are seen in the spleen. The masses are rarely of larger size than a Spanish nut.

(γ) **Actinomycosis** occurs somewhat more rarely in the liver than it does in the other tissues which it affects in man. It leads to the formation of ragged abscesses which are traversed generally by a number of trabeculæ composed of the undestroyed pre-existing connective tissue and vessels of the affected portion of liver. The condition, therefore, has a certain resemblance to pylephlebitis. The abscesses are generally large, and send numerous processes of inflammatory tissue which has not, as yet, broken down into the surrounding structure. Microscopically, the appearances are those seen in other cases of actinomycosis. The condition may be surmised from the general appearance of the liver, but a diagnosis cannot be made on these lines alone. It is only when the definite nodules of the fungus itself are proved to be present by aid of the microscope that the nature of the change can be affirmed without doubt. It is probable that, in addition to actinomycosis, the liver is occasionally the seat of other forms of streptothrical infection.

(4) **Chronic fibroses.**—Apart from the formation of scars in the liver, such as we have seen to occur in the terminal stages of gumma, we meet with three distinct varieties of fibrotic change in the liver. The alterations which they produce in the macroscopic appearances of the organ are alone sufficient to justify the separation of the chronic fibroses into different classes.

(*a*) **Multilobular fibrosis or cirrhosis.**—In this variety the fibrous tissue is very irregularly distributed throughout the organ, and by its contraction leads to a great diminution in the size of the liver. On this account the change is often called **atrophic cirrhosis**, the name 'cirrhosis' being derived from the *yellow* colour of the organ due to the presence of confined bile. At the same time the fibrous tissue in its contraction causes an irregularity of the surface of the organ, and has given rise to the name of 'hobnail liver.' Lastly, in accordance with the belief that this variety of cirrhosis is principally caused by over-indulgence in spirits, the change has been termed 'alcoholic cirrhosis,' or, more specifically, 'gin-drinker's' or 'whisky-drinker's' liver.

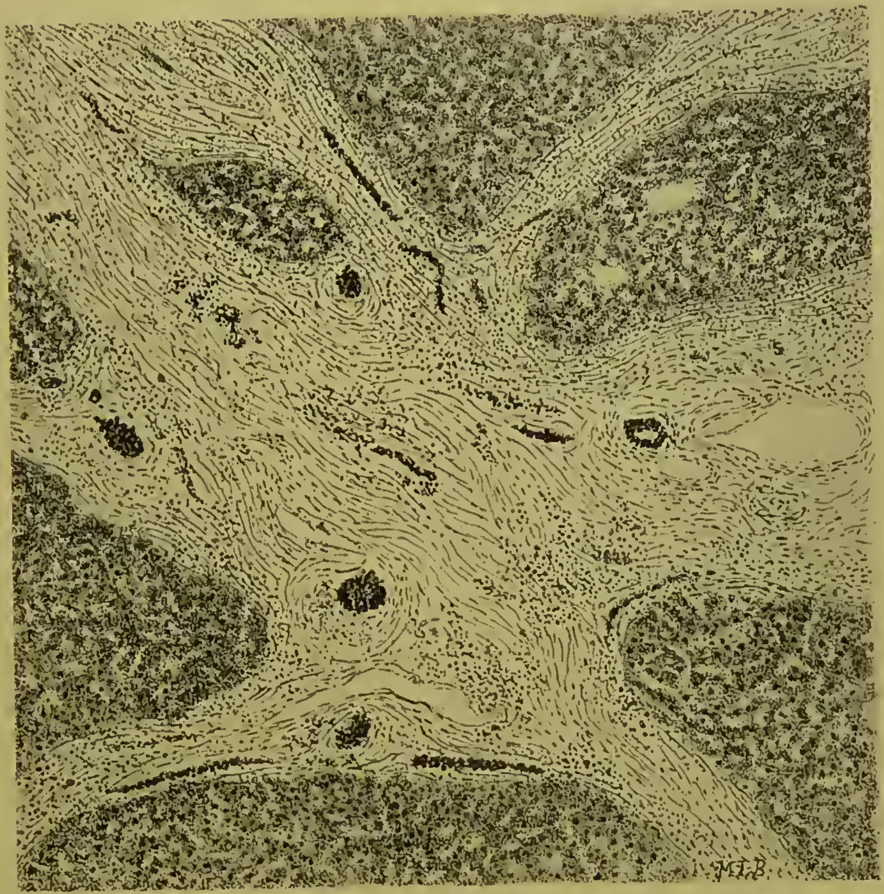


FIG. 103.—MULTILOBULAR OR ATROPHIC FIBROSIS OF THE LIVER. × 80.

An irregular mass of dense fibrous tissue passes through the section dividing the liver tissue into more or less rounded masses of varying size. The new fibrous tissue shows a considerable number of connective-tissue cell nuclei, and new bile ducts, some of which are cut transversely, but the majority longitudinally. The latter have the appearance of a narrow line of deeply staining nuclei.

The fibrous tissue in cases of multilobular fibrosis runs in broad bands throughout the entire substance of the organ, and its more definite bands may easily be seen on the surface of a section, interlacing with one another and cutting up the liver substance into a number of irregularly polygonal areas of different, but usually small, sizes. The fibrous tissue itself is grey in colour and semi-translucent, and that which is present in the depth of the organ can easily be seen to be in direct connection with the thickened capsule of the liver itself. The fibrous tissue is especially developed in connection with Glisson's capsule and its prolongations through the organ, but it is not confined thereto. For careful examination shows that there is a considerable new formation of fibrous tissue which, though it may have originated in connection with the periphery of a lobule, nevertheless strikes out in directions that have no definite relation to the lobules themselves, but in many instances pass right through the centres of them.

The effect of the presence of this large increase in the amount of fibrous tissue in the liver not only leads to a diminution in the size and weight (an atrophic liver of this kind may weigh only two pounds, in spite of the large amount of fibrous tissue present), but it also leads to a considerable increase in the density of the organ. This may be so great that it is impossible to break down the substance of the organ by any pressure that is applied by the finger, and is in great contrast to the ease with which a normal liver breaks under a slight pressure. The contraction of the fibrous tissue, too, leads to a compression of the portal and biliary canals, and accounts for the ascites, the yellow colour of the hepatic tissue, and the slight amount of jaundice that are met with in the disease. At the same time the liver cells themselves undergo a pressure atrophy, and the actual amount of liver tissue that is present in an advanced stage of the change is very small.

Microscopically, the changes in multilobular fibrosis are just what might be expected from a careful examination of the naked-eye appearances. But in addition there are certain changes that could not have been anticipated.

The connection of the fibrous-tissue strands in the substance of the organ with the capsule is easily recognisable in a microscopic section, and the explanation of the 'hobnail' appearance becomes clear. For it is seen that the capsule is not equally thickened everywhere, but is fairly thin at points where there is no connection with strands from the interior of the organ, and is proportionately thick at points where such connection obtains. In the process of contraction of the fibrous tissue, therefore, the capsule tends to be drawn in at certain points, while the relative laxity of the capsule at other points allows of the slight extrusion of those portions of liver tissue which are being compressed on all other sides. This explains the appearances satisfactorily, but it is doubtful whether it is the whole explanation. It has been shown that there is a tendency for the new formation of true hepatic substance in these situations, and it is probable that the protuberances on the surface of a fibrotic liver are not merely due to altered distribution of pre-existing liver substance, but are also due to definite new formation of liver cells.

In the strands of fibrous tissue there are always to be seen collections of cells which are arranged in parallel strings consisting of two lines closely apposed. A single pair of the strings of cells gives an appearance very similar to that of a small portion of a Henle's loop in the kidney. Although there is the greatest divergence between the views of different authors, the tendency at the present day is to believe that the appearances are due to the definite new formation of tubes which are designed to functionate as bile ducts, and that they are formed at the expense of true liver cells which modify their function for the purpose.

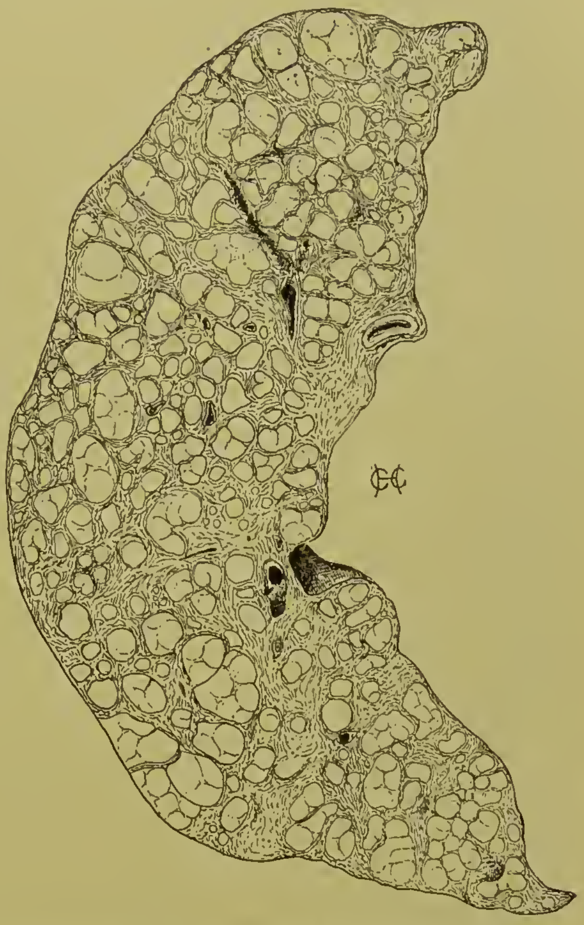


Fig. 104.—Multilobular Fibrosis of Liver (Post-syphilitic ?) × $\frac{2}{3}$.

The condition shows extreme atrophic fibrosis. The irregular colourless portions consist of hepatic substance much compressed, and fatty. The rest of the organ practically consists entirely of very dense fibrous tissue. The specimen was obtained from a child aged nine years.

As a rule, a striking appearance in the case of a fibrotic liver is the amount of fat that is present. It is difficult to say whether the fat globules which are present in the liver cells are the result of infiltration or of degeneration. There are reasons for and against each view. But there is no doubt that when the amount of fat in the remaining liver substance is great, the actual amount of true liver substance which is left is exceedingly small. For the liver cells undergo a pressure atrophy from both sides; not only are they compressed by the contracting fibrous tissue, but they are also compressed by the droplets of fat. As a result of the combined change, it may be almost impossible to recognise the tissue microscopically as liver at all.

Besides the new formation of fibrous tissue it has been shown (Flexner) that in this variety of cirrhosis there is a considerable new formation of yellow elastic tissue.

Before leaving the subject of atrophic fibrosis, it must be mentioned that there is occasionally met an exquisite example of the condition which, nevertheless, differs in many points from the ordinary variety which has been described above. The ordinary or alcoholic cirrhosis occurs chiefly in adults, as might be supposed, but the variety to which attention is now being drawn occurs in children. It may be met with as early as four or five years of age, but its commonest incidence is between the ages of eight and sixteen. The degree of fibrosis in these cases is such that its equal is very rarely seen amongst adults. In other respects the liver changes are identical in the young and in the old. It is probable that it is a post-syphilitic change of congenital syphilis.

Into the question as to whether cirrhosis of the liver generally may not be due to the effect of infective or other agents derived from the intestine we shall not enter here. It will suffice to say that there is a considerable amount of evidence to show that certain varieties of multilobular fibrosis, at all events, are of bacterial origin.

(*b*) **Unilobular fibrosis or cirrhosis.**—Concerning this variety of hepatic fibrosis there is much more doubt than concerning either the multilobular or the intercellular varieties. The type is far less common than either of the two other varieties.

In its theoretical form unilobular cirrhosis of course is characterised by the new formation of a fibrous tissue which surrounds the individual lobules. Such a condition, however, is hardly ever seen, although we undoubtedly meet with cases in which the adventitious fibrous tissue forms a far closer meshwork than it does in the multilobular type. At the same time it must be allowed that there is a variety of hepatic fibrosis which is associated with an increase in the size of the liver ('hypertrophic cirrhosis') instead of a diminution ('atrophic cirrhosis'), and that the surface of the organ in this variety is fairly smooth, or at most finely granular, and not coarsely granular or 'hobnailed.' The increase in the size of the organ in this variety is beyond question, for the liver may weigh five or six pounds. It is moreover different from the multilobular variety in colour, being usually of a deep red and not pale or yellow.

When we come to examine a section of such an enlarged liver microscopically, we find that there is present a very definite fibrosis of the fine-meshed kind that has been referred to above. The actual strands of the fibrous tissue are not very wide, but they are of fairly even width throughout the organ. In this respect they offer a marked contrast to the strands of fibrous tissue in atrophic cirrhosis. It is undoubtedly true, moreover, that the general tendency is for the fibrous tissue to be arranged around the individual lobules. Nevertheless we shall not have to seek far to find a spot at which the strand of fibrous tissue cuts right across a lobule, as it so frequently does in the atrophic variety.

In spite of some differences, therefore, the unilobular has many resemblances to the multilobular variety, and some authors have maintained that the atrophic is a late stage of the hypertrophic, or, conversely, that the hypertrophic fibrosis ends by becoming atrophic. On the other hand, the majority of authors maintain that the two varieties are completely distinct not only in appearance but also in causation. They hold that the unilobular variety is especially bound up with changes that start in the bile ducts, and upon this view speak of the condition as a 'biliary' cirrhosis.

That this view is a possible one is seen from the fact that the fibrous tissue is particularly well developed in those regions of the liver at which the bile ducts are present, viz. at the periphery of the lobules. Further, there is no doubt that unilobular fibrosis is associated with the presence of a large number of those cellular appearances which we have said are to be regarded as newly formed bile ducts.

The fibrous tissue present in cases of unilobular cirrhosis is not so dense and contains a larger number of nucleated cells than is the case in multilobular cirrhosis. For this reason the condition can more easily be regarded as being of inflammatory origin The cells themselves are not merely young connective-tissue cells, but large numbers of small round cells, presumably leucocytes, are also present. It is of course impossible to determine whether these cells are to be regarded as indicating that the condition itself is essentially inflammatory, or whether it simply means that the newly formed fibrous tissue has itself become the subject of inflammation as the result of the action of an irritant which is acting on it from the bile ducts or the vessels or the hepatic cells themselves.

(*c*) **Intercellular fibrosis or cirrhosis.**—This variety of hepatic fibrosis is met with exclusively in stillborn fœtuses and infants that are the subjects of congenital syphilis. It has, therefore, also received the name of **syphilitic** cirrhosis.

The liver in these cases is larger than normal, is generally of a bright yellow colour, and is of a leathery hardness. It shows little or no irregularity of the surface, but nevertheless the amount of fibrous tissue present may be so great that it is recognisable macroscopically. Under the microscope the fibrous tissue is seen to be situated not only at the periphery of the lobules, but also to penetrate into it and lie between the individual liver cells. In many cases the intercellular substance is fully formed fibrous tissue, but in others it is rather fibroblasts which lie between the hepatic cells than fully formed fibrous tissue. In any case the actual picture produced is one which is totally unlike normal liver. For the liver cells become compressed into irregular polygonal areas of different sizes and shapes, and the lobular

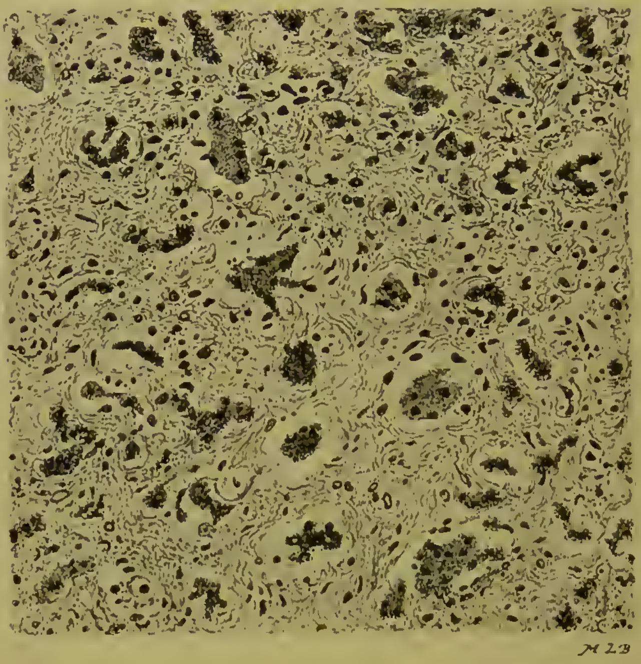


FIG. 105.—SECTION OF INTERCELLULAR FIBROSIS OF LIVER (CONGENITAL SYPHILIS). × 420.

The irregular dark masses are compressed hepatic tissue. The rest of the section consists of dense fibrous tissue, in which but few connective-tissue cells are present.

arrangement of the liver is lost. At some points the amount of fibrous tissue may be greater than at others, but in the main the distribution is fairly even over the whole liver. Bile ducts and vessels are compressed, and singularly few of them are visible at all. Such bile ducts as are present are stained a brilliant yellow by the confined bile, and the liver cells themselves take on the same colour, owing to diffusion of bile pigments into them. This colour of the liver in congenital syphilitic cirrhosis is not, however, constant.

Sometimes the variety of cirrhosis which has been just described is conjoined with a certain amount of fibrosis of the multilobular type. These cases form a connecting link between the typically syphilitic fibrosis and those cases of multilobular fibrosis which we have termed post-syphilitic.

(5) **New-growths.**—The liver is liable to be the seat of a variety of new-growths, but the malignant are more commonly met with than the non-malignant, and secondary growths more common than primary.

Of non-malignant growths only one—the cavernous angeioma—is at all common in the liver. Fibromata have been described, but are rare. Adenomata occur, and are undoubtedly sometimes found in the non-malignant form, but far more commonly they pass over the border between non-malignancy and malignancy and become definitely carcinomatous.

Cavernous **angeiomata** in the liver are generally of small size, rarely being larger than a walnut. They are situated in the superficial portions of the organ, and their outer surface lies flush with the general surface of the liver, so that when the organ is removed the angeioma appears as a stain rather than as a tumour. On section they are roughly quadrilateral in shape, having in this respect resemblances to a hæmorrhagic infarct of the liver, and are built up of large blood spaces. They do not give rise to symptoms and are of no clinical importance.

Adenoma of the liver occurs in normal and in cirrhotic livers as solitary or multiple greyish-yellow masses which are usually of small size. The smallest nodules do not seem to be provided with a capsule, but the larger nodules have generally a well-defined capsule. Histologically, the growths may consist of a number of convoluted and branched ducts or of irregular hepatic tissue contained in a more or less voluminous connective tissue. The growth is a very rare one.

Malignant growths of the liver are almost always carcinomatous, and then they may be primary or secondary.

Primary carcinoma of the liver is very rare. It shows itself under four forms. In the first there is only one mass, or at most two or three. This mass is generally found in the right lobe and is of considerable size; it extends radially. From its appearance it has been termed 'massive cancer.' In the second variety metastases are formed in the liver itself. This gives rise to the 'nodular cancer.' The third variety is associated with a cirrhotic condition of the liver, and the masses of carcinomatous cells lie between bands of dense fibrous tissue. The organ, generally, has the appearance of an atrophic cirrhosis. This is the 'cancerous cirrhosis' or 'cancer with cirrhosis.' The fourth variety is one which starts in connection with the portal canals and travels along them, sending out offshoots into the hepatic tissue generally. In this variety of hepatic carcinoma definite nodules of a grey

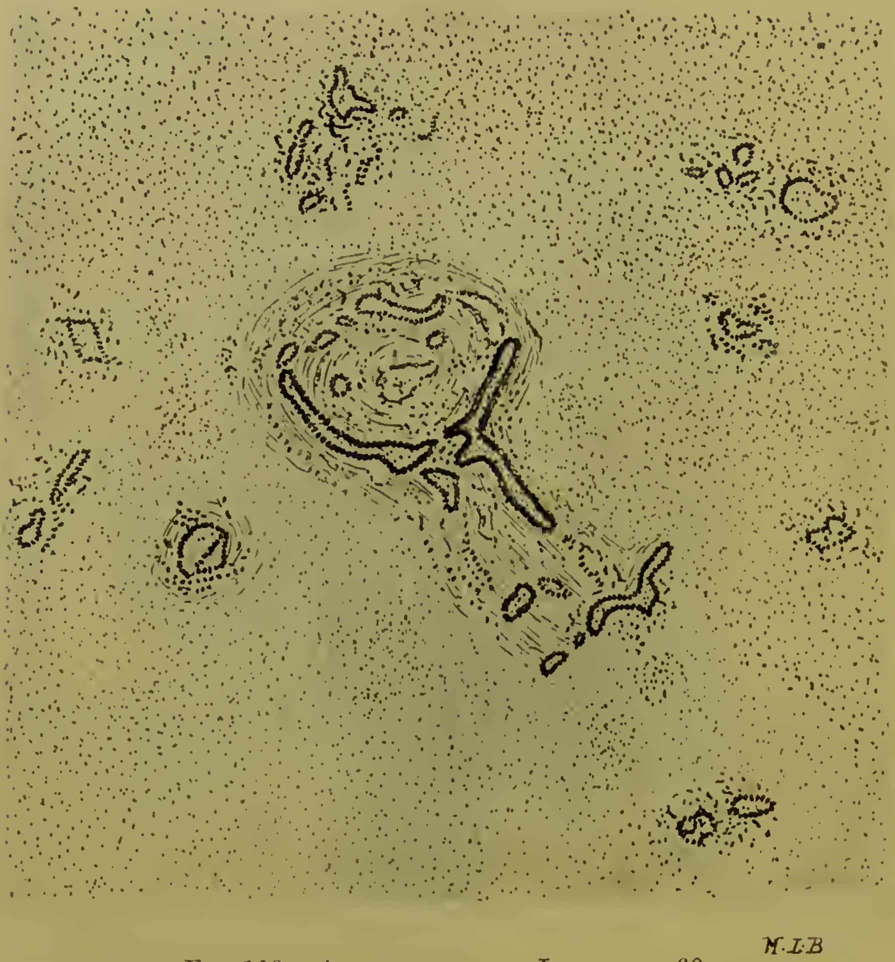


Fig. 106.—Adenoma of the Liver. × 60.

Discrete masses of tissue are present throughout the organ, which consist of a greater or less quantity of fibrous tissue with irregular duct-like formations. By some authors the condition is termed 'congenital cystic disease,' and it is certain that sometimes the 'ducts' become dilated into 'cysts.'

colour are usually present, but sometimes the appearances are very similar to those seen in cancer with cirrhosis.

According to the character of the growth, the liver affected with primary carcinoma is soft or hard. When the nodules are of relatively large size, they often undergo softening in the centre. If the nodule itself is situated on the surface of the organ, this softening leads to umbilication of the nodule, a very characteristic feature of carcinomatous nodules in the liver, whether primary or secondary. On the other hand, when the liver is intensely fibrotic, the fact that one has to do with a carcinoma is frequently only first recognised when microscopic sections have been examined.

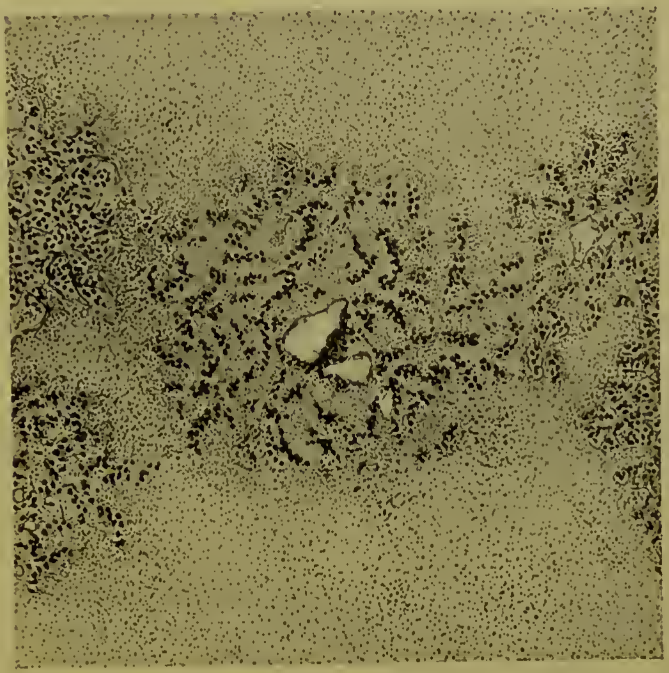


Fig. 107.—Primary Spheroidal-cell Carcinoma of Liver. × 45.
The growth is distributed chiefly around the branches of the portal vein, and has a racemose arrangement.

Histologically, the primary carcinomata of the liver are almost always composed of spheroidal cells. Sometimes one meets with cases that are more of an adenomatous type, and then German authors refer to the condition as **adeno-carcinoma**. The principal difference depends upon the question as to whether the growth has started in connection with truly hepatic cells, or in connection with the bile ducts. In the latter case we are most likely to meet with either a typical columnar-cell carcinoma, or a carcinoma of a transitional type. Confusion must not be made here with carcinoma that starts definitely from one of the larger bile ducts. With this variety of malignant growth affecting the liver primarily we shall have to deal later. The bile ducts that are here to be understood are those of microscopic size, and lie close to the bile canaliculi.

In **secondary carcinoma** of the liver we find a considerable uniformity amongst cases. The main difference lies in the number and the size of the secondary nodules themselves. Sometimes they are so numerous that there is little normal liver substance left, and the size of the organ itself is greatly increased. In other cases we find only one or two nodules, which are, perhaps, no larger than peas. The nodules may be situated in the substance or on the surface of the organ, and in the latter case they generally show marked umbilication, and give a very irregular shape to the surface of the liver. At first the nodules are discrete, but when they have been in existence for some time, and have grown circumferentially, two or more nodules may coalesce at their margins.

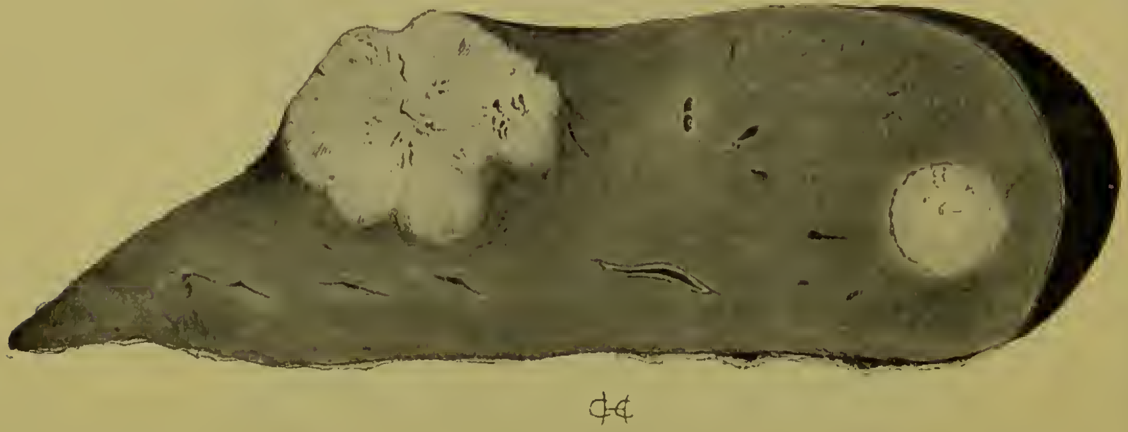


Fig. 108.—Secondary Nodules of Carcinoma in Liver. × ¾.
The nodules show a fairly sharp outline, though microscopically it is seen that they are without capsules. The 'umbilication' of the superficial nodule is well shown.

Macroscopically, the nodules are almost always of a creamy colour, and frequently of a creamy consistency. They seem to be very sharply defined from the liver tissue in which they lie, although they do not appear to be surrounded by a capsule. Microscopically, it is seen that, although the border of the growth is a fairly well-defined one, yet the edge is not perfectly regular. Moreover, although there is no formation of a capsule, yet the liver tissue surrounding the nodule shows signs of irritation, and the hepatic cells signs of pressure atrophy. Hence there is a more or less definite zone around the nodule which recalls closely the line of small cell infiltration which lies in advance of the spreading margin of a primary malignant new-growth (e.g. a carcinoma of the breast).

Secondary nodules of malignant growth in the liver, of course, always possess the characters of the primary growth. Thus one may meet with columnar-cell carcinoma when the primary growth has been in the intestine, or squamous-cell carcinoma with well-developed cell nests when the primary growth has been in the œsophagus. Sarcomata far more rarely form secondary growths in the liver than carcinomata, but occasionally they are found, and then they may be composed of any kind of cell which goes to the building of a sarcoma.

Primary sarcoma of the liver is excessively rare, but the changes which it induces are marked. The organ is nodular, greatly enlarged, weighing perhaps ten pounds, and in it are many masses of a soft growth, which is often reddish brown, from admixture of broken-down extravasated blood. As a rule, the small amount of liver substance which is left is of a brilliant green colour from the contained bile. The microscopic characters are often very complicated, and, owing to the extreme rarity of the condition, we shall not delay to consider them.

Amongst the new-growths, although it hardly belongs to the group in strict fairness, we may include a rare condition, viz. **congenital cystic disease.** The change has certain resemblances with congenital cystic disease of the kidneys, and the two are sometimes found in conjunction. Macroscopically, a congenital cystic liver shows, dispersed throughout its substance, a number of small cysts. The number of these cysts differs considerably in different cases, but is rarely very large. Nor are the cysts themselves large, in this respect differing from the cystic disease of the liver which depends upon the formation of adenomatous growths in connection with the bile ducts, and which we shall describe later. It is probable that they are, in reality, abnormal bile ducts. Upon this point, however, it is impossible to speak with certainty.

Cysts.—The most important variety of cyst which is found in the liver is that caused by the presence of **hydatids.** A hydatid cyst may be of practically any size, some of the largest containing a pint or more of fluid and being as large as a child's head. They may be single or multiple, but it is commoner for only one cyst to be present. The hydatid cyst itself must be differentiated from the wall of the cavity in which the cyst lies. The former is an integral portion of the parasite, the latter is produced at the expense of the hepatic tissues and forms a veritable capsule.

The cyst wall has a very characteristic composition. It consists of a hyaline material in which are to be seen a number of fine lines lying parallel to one another. In an old cyst we may find that calcium salts have been deposited in the cyst wall, or that it has become modified by the extension to it of suppurative processes going on in the liver tissue which bounds it. The capsule in which the cyst lies, on the other hand, consists of more or less fully formed connective tissue which may be comparatively free from cells, or, if it is the seat of a definite irritation, may be infiltrated with exudation fluid and a large number of leucocytes. Although the capsule is dense and smooth on the side towards the parasite, it shades off more or less imperceptibly into the normal liver tissue externally.

The hydatid cyst contains usually a number of daughter cysts, and these, in their turn, may contain other daughter cysts. At the same time it is probable that at some points on the wall of the mother cyst or on the daughter cysts or of both, small sessile growths will be found which are ultimately destined to become daughter cysts. In the smallest cysts of all will be found the parasites themselves, attached to the cyst wall. Whether parasites are found attached to the wall of the mother and the larger daughter cysts depends upon circumstances. Sometimes they are found thus attached, but more commonly no parasites are found here, although the cystic fluid contains hooklets that have become detached from parasites that have undergone degeneration.

Reference has already been made to the changes that may be undergone by hydatid cysts (p. 456).

B.—THE BILE PASSAGES

The commonest affection of the bile passages consists in the formation of gallstones. These concretions may be without great effect upon the bile passages themselves, or they may lead to the most profound changes.

Gallstones.—Speaking broadly, gallstones are of two kinds, those consisting of cholesterin, and those consisting of bile pigments. It is, however, very rare to find that a calculus consists of either of these substances alone; more commonly both are present, though the one or the other is present in vastly preponderating quantity.

Cholesterin gallstones are of two kinds. Either they are multiple, moderately small, and of fairly equal size, facetted, and covered externally by a thin layer of brown or black material, or they are round or oval, single, faintly stained with yellow bile, semi-translucent, and fairly large. Gallstones of the first kind constitute by far the greater number of those found; single cholesterin gallstones, corresponding to the second variety mentioned, are among the rarest of gallstones. The facetted gallstones are opaque, but this is due to their outer covering; when they are split, it is seen that the internal portion consists of a colourless crystalline material that cuts easily and has a greasy feel. This material is practically pure cholesterin. The single cholesterin calculus is composed of this cholesterin alone, and has a beautiful crystalline appearance. In the case of both kinds of cholesterin gallstone the actual nucleus of the calculus is composed of some organic material upon which the crystals are deposited. This organic nucleus is generally more considerable in the case of the multiple facetted gallstones than in the case of the single ones. The outer covering of the facetted gallstones consists of calcium carbonate, with an admixture of bile pigments. It is, however, present in so small quantity, that the determination of its actual composition in any individual case is a matter of great difficulty.

Gallstones with a composition of bile pigment have a totally different appearance from those composed of cholesterin. They are always small and multiple, are of an intense jet black colour, and are never facetted, but are always irregular and nodular. They crumble very readily, and are of a non-crystalline structure. They consist principally of a combination of bilirubin and biliverdin with calcium.

The above form the large majority of biliary calculi. In very rare instances calculi composed of other substances are found (e.g. calcium carbonate), but they need not detain us.

The commonest situation in which gallstones are found is the gall bladder. Even when they are present elsewhere it is decidedly rare to find the gall bladder completely free. The reason of this is that the gall bladder is the general seat of their formation. It is, however, not the only seat at which they are formed. For in a certain number of instances we find them in the larger bile ducts, constituting the so-called ‘intra-hepatic’ gallstones. It is, of course, possible that the calculi should be found in the cystic duct or the common bile duct before or after its junction with the pancreatic duct. This is, in fact, only a manifestation of the tendency of the gall bladder to expel its contents. The question as to the actual position in which the gallstones are found depends upon their size and upon the size of the ducts themselves. From the smallness of the lumen of the cystic duct, it is quite possible that the calculi will be found in the gall bladder alone; if they have passed into the cystic duct, it is probable that they will be able to pass along its entire length and into the common bile duct, but they are very likely to be arrested at the orifice of the duct on the papilla in the duodenum. When they have reached the latter point, they may dilate the duct, and thus make their way into the intestine, or, if they are of any considerable size, they may reach the intestine after ulcerating through the mucous membrane of the duodenum at the papilla.

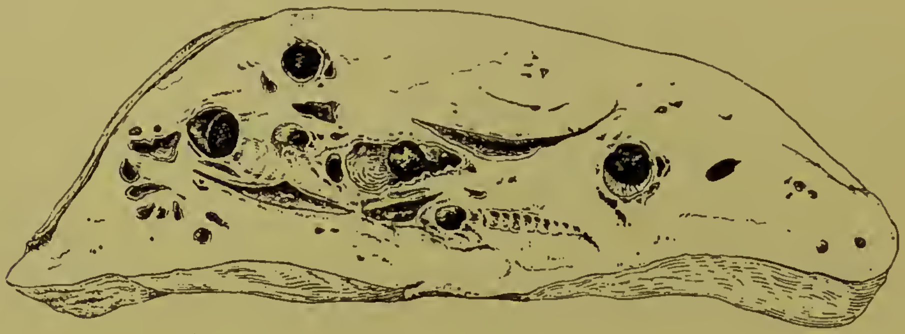


Fig. 109.—Intra-hepatic Gallstones. × $\frac{2}{3}$.

The bile passages throughout the organ are enormously dilated, and in many of them are seen dark more or less rounded concretions.

When a gallstone has reached the intestine the symptoms which it causes generally cease. But in some cases in which the calculus is of abnormal size, it leads to definite intestinal obstruction and calls for immediate operation. A calculus thus removed from the intestine after leading to intestinal obstruction is found to have received additional coats of fæcal material which have notably increased its size.

With regard to the occurrence of jaundice in cases of gallstone or other biliary obstruction, it is clear that the condition can only occur if the bile gains access to the blood instead of passing, as normally, into the intestine. This can only happen if the right and left hepatic ducts or the common bile duct are blocked. Gallstones may be present in the gall bladder or in the cystic duct, and may give rise to other symptoms, but they can never give rise to jaundice. Conversely, it is clear that any obstruction to the common bile duct gives rise to jaundice, and that jaundice, though very frequently found in connection with gallstone, is not pathognomonic of the latter condition.

Gallstones are not without their effects upon the tissues with which they are in contact, and when they are placed in such a position that they obstruct the entire flow of bile from the liver, they lead to changes throughout the whole system of bile ducts and the liver cells by which the bile is formed. So far as is known, however, all the effects of gallstones are mechanical.

The local effects of gallstones may be insignificant or severe. The commonest and least significant change which they induce is in the gall bladder. Whenever gallstones are present in the gall bladder there is an alteration in the consistency of the bile which it contains. It becomes far more syrupy and ropy, and frequently it becomes of a paler colour. The reason of this change lies in the fact that the irritation of the wall of the gall bladder causes it to excrete a larger amount of nucleo-proteid than normal. This material, which has so close a resemblance to mucus that it has generally been described as being actually that substance, is in cases in which the number of gallstones is considerable, or in which a gallstone is impacted in the cystic duct, the only material found in the gall bladder; bile pigments are completely absent, and the gall bladder contains, besides the calculi, a smaller or greater quantity of a mucus-like substance alone.

In other cases the irritation caused by the calculi goes further. It leads to a definite inflammation of the gall bladder (**cholecystitis**), and then a whole series of changes may be induced. The condition may go on to the formation of adhesions between the gall bladder and the abdominal wall, or there may be formed a large mass of dense adhesion in the portal fissure, or the gall bladder may become so full and its walls so altered that it ruptures into the peritoneal cavity and produces a general peritonitis, or, again, the inflammation may go on to suppuration with the formation of an abscess which either ruptures into the peritoneum or externally or perhaps into the intestine. It must not be supposed, however, that all cases of cholecystitis are due to the presence of biliary calculi, for this is not so. In many instances the condition seems to have been induced by the action of an irritant which has reached the gall bladder by travelling up the bile passages from the intestine.

By far the most important effect of gallstones is the formation around them of a mass of **carcinoma**. Although it is not in the greatest number of cases in which we meet with gallstones that we find carcinoma of the gall bladder, it is undoubtedly true that in almost every case that is met of carcinoma affecting the gall bladder or the bile ducts, gallstones are, or have been, present. Were it not for some cases of primary cancerous disease of the main bile ducts, and of cases in which no gallstone is actually found in the centre of a mass of carcinoma that occupies the situation of the gall bladder, we might say that the evidence afforded by cases of gall-bladder carcinoma in favour of the mechanical origin of carcinoma is overwhelming. As a matter of fact, it is probable in many cases of carcinoma of the gall bladder in which no calculus is found, that the calculus has disappeared owing to the central disintegration of the cancerous mass; such a condition of central disintegration is very common, and in some instances the central cavity must be looked upon as the representative of the former cavity of the gall bladder. Occasionally one does not find a definite calculus in the centre of the mass of carcinoma, but only a gritty material principally composed of bile pigment.

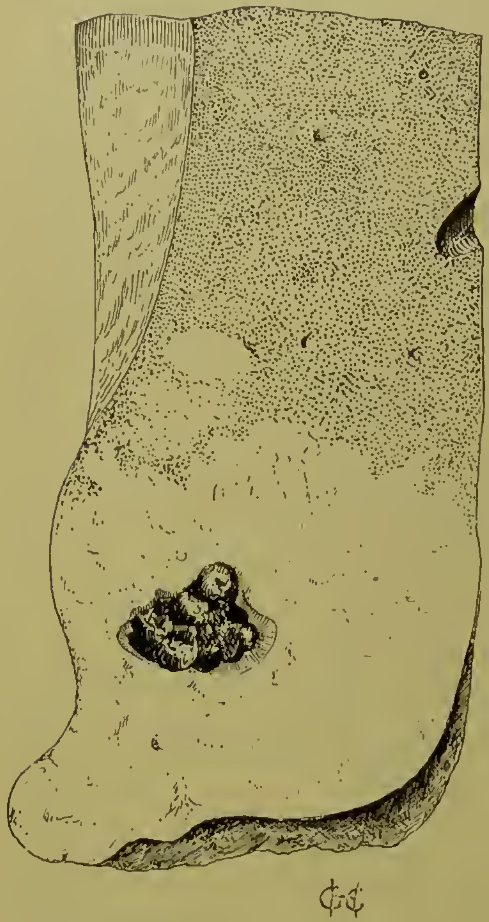


Fig. 110.—Carcinoma of Liver commencing round a Gallstone. $\times \frac{5}{6}$.

Probably the mass of cancer represents the gall bladder. It occupies the situation of the gall bladder, and no gall bladder was found at the autopsy. The growth is of the columnar-cell variety, a point in accordance with the above view.

Carcinoma of the gall bladder is almost always of the columnar-cell type. As a rule, the arrangement is fairly typical, but sometimes the epithelium shows a tendency to assume the transitional flattened type which is normally present in the gall bladder. The growth extends laterally, and invades the liver to a greater or less extent. In an early case we may imagine that we have only to do with a chronically thickened wall of the gall bladder until microscopic sections are examined. In other cases the growth forms a mass as large as the fist. Secondary nodules are formed in the lymphatic glands, in the hilum of the liver, and in the liver substance itself, but this is hardly so common as for the primary growth to be the only one.

The *bile ducts* are not nearly so frequently affected by morbid conditions as the gall bladder, and even when they are affected the conditions are generally induced in them secondarily. Primary morbid conditions of the bile ducts, in a strict sense, are excessively rare.

The commonest affection of the bile duct concerns the common duct, and consists in the extension to it of an acute catarrhal inflammation of the mucous membrane of the intestine. As a result of the inflammation the mucous membrane around the orifice, in the ampulla of Vater, and along the entire length of the duct, becomes red and swollen. It pours out a greater amount of mucus than normal, and the epithelial cells desquamate. As a result of these changes the lumen of the tube becomes blocked. For this reason catarrh of the bile duct is one of the commonest causes of jaundice. After a few days the condition usually undergoes resolution.

The ampulla of Vater is the occasional seat of a carcinomatous growth. The entire mass is rarely larger than a pea, but its situation is such that it is accompanied by the most profound jaundice. Nevertheless the orifice of the duct may not be completely blocked, so far as can be determined by exerting pressure on the gall bladder at the autopsy. Cases of this description are generally accompanied by fever and certain other somewhat anomalous symptoms. Secondary growths are rare.

Carcinoma also affects the bile duct within the liver on rare occasions. Reference is not here made to those cases in which the bile ducts become secondarily affected by extension of a carcinomatous mass that has commenced either in the liver or elsewhere as its primary seat, but to cases in which the bile duct is the primary seat of growth itself. The growth may be a more or less typical columnar-cell carcinoma, but sometimes it is an 'adeno-cystoma.' That is to say, it may consist of a fibrous-tissue stroma with numerous clefts and spaces which are lined by a single layer of cells having the character of endothelial cells, and which are frequently dilated to form definite cysts that may be of large size. It is not always the case, however, that an adeno-cystoma having the histological characters mentioned in its solid portions goes on to the formation of cysts. Growths of this kind may form many metastases in the liver itself which have the characters of the primary growth.

Apart from the varieties of obstruction which have been mentioned above, we sometimes meet with a definite stenosis of the bile ducts as the result of the formation of a mass of connective tissue of inflammatory origin. This condition is rare, and it generally occurs in children that are the subjects of congenital syphilis or have family histories consonant with such an assumption. In these cases either we may meet with the formation of a mass of fibrous tissue in the hilum of the liver, which we may assume results from the absorption of a former gumma, or we may actually find that a septum has been formed across the bile duct which completely obstructs it. In either case the condition must be regarded as, so to speak, accidental.

In all the cases of obstruction to the bile ducts that have been mentioned a series of effects is to be noticed in the ducts behind the obstruction and in the liver itself. These effects are independent of the actual cause of the obstruction, and therefore they may be considered together.

The most noticeable change is an alteration in the colour of the liver. Instead of being of a reddish-brown colour, it is either a deep olive green or some colour intermediate between this and yellow. The organ is also generally enlarged, and sometimes the enlargement is considerable. On making sections into the organ, it is found that the bile ducts are everywhere enormously dilated. There is not the great difference that normally obtains between the right and left hepatic ducts and their tributaries, but throughout the liver there are ducts that have perhaps a diameter equal to that of the little finger. These dilated ducts reach almost up to the surface of the liver and seem to end more or less abruptly.

Considered individually, the changes in the ducts are seen to be accompanied by a thickening of their lining membrane which may lead to their being mistaken for branches of the portal vein. Microscopically there is a definite increase in the thickness of the wall, and particularly in the amount of fibrous tissue present. The epithelial lining is usually completely wanting.

The main ducts may or may not contain bile, but in the case of the smallest ducts there is no doubt that they not only are dilated, but are also filled with inspissated bile. This is well seen in microscopic sections, for the deep green bile pigment is found everywhere in the section lying in masses which correspond to the dilated ducts. The bile also diffuses to some degree into the liver cells themselves. In many instances they have a definite green tinge.

The liver cells, in addition to being infiltrated with bile pigment, also undergo a marked atrophy from the pressure to which they are exposed. This atrophy is not, however, generally so marked as it is in cases of chronic venous congestion.

SECTION XI

THE PANCREAS

THE morbid conditions specially affecting the pancreas are not numerous, and, even secondarily, the organ is but rarely affected.

Of inflammatory conditions the pancreas is liable to two, viz. abscess and an inflammation so intense that it rapidly ends in gangrene.

Abscess of the pancreas is rare, but it may occur in connection with a gastric or a duodenal ulcer. It is naturally formed most commonly in the head of the organ, and rapidly points and breaks into the ulcer, so that it becomes itself a part of the gastric or duodenal ulcer and forms its floor. Not infrequently the suppuration in the pancreas is associated with a suppurative peritonitis in the immediate neighbourhood which is equally the result of the ulcer.

Gangrenous pancreatitis is a rare and formidable complaint. It is hardly to be diagnosed during life, and after death it is difficult to determine owing to the general inflammatory condition of the parts in the neighbourhood of the pancreas. When the inflammatory material has been removed, the altered pancreas is found to be represented by a flabby mass which looks like dirty wash-leather, and is only recognised as being the organ by its position. Microscopically, there is no longer visible any trace of the true glandular substance. All that is left is merely the fibrous supporting meshwork of the gland, and even this is devoid of any definite structure. The destruction of the gland apparently takes place very rapidly, for cases in which it is found after death have always run a particularly rapid course associated with high fever. There is little doubt that the disease is due to an intense microbial action, but more than this cannot at present be said. Accompanying the condition it is usual to find evidences of fat necrosis.

The pancreas is found to undergo change in a considerable proportion of cases of diabetes mellitus. The commonest change is a **fibrosis** accompanied by atrophy, which leads to a reduction of the weight of the gland from about three and a half ounces to perhaps two ounces or less. Not all cases of diabetes are accompanied by changes in the pancreas, and even when the pancreas is affected, the change is not always a fibrosis with atrophy. Sometimes it is found that the entire gland has become replaced by a mass of carcinoma. In any case, however, it is certainly necessary that, whatever the change, the whole organ shall have been changed. The existence of the merest trace of normal functionating pancreatic tissue seems to prevent the occurrence of diabetes.

When fibrosis and atrophy are present, the gland is not only harder than normal and macroscopically smaller, it is also microscopically the seat of a great increase in the amount of fibrous tissue, and a corresponding diminution in the amount of substance which bears a resemblance to normal gland tissue. The increase in the fibrous tissue takes place principally in the fibrous stroma. The trabeculæ that traverse the gland are enormously thickened, and bands of dense fibrous tissue pass in all directions through the organ compressing and replacing the true glandular tissue. The gland substance itself is notably diminished in quantity, and it is doubtful whether any of the material which under the microscope resembles pancreatic tissue anatomically, is capable of exercising its function. Such, at least, is the conclusion to which we are led upon experimental grounds.

Under many conditions the pancreas is much harder than normal without having undergone, so far as can be determined, any fibrotic change. Such are cases of chronic heart disease, cirrhosis of the liver, and, generally, conditions in which the occurrence of ascites is common. What the actual change is that leads to this marked hardness of the organ, it is difficult to say, but the fact can at once be recognised by touch.

New-growths of the pancreas, other than carcinoma, are very rare, and even carcinoma is uncommon. When it occurs, it may be primary or secondary, and the one variety is about as common as the other. Primary carcinoma may affect either the head or the tail of the organ exclusively, or the disease may commence in the one part, usually the head, and spread thence until it has involved the whole. Sometimes the gland does not, at first sight, appear to be greatly altered; in other cases the diagnosis is at once clear from the large mass which has softened in the centre, and which occupies the normal situation of the pancreas. When the head of the pancreas is affected, it is common to meet with deep jaundice from the interference which the growth interposes in the way of the flow of bile into the intestine.

Carcinoma of the pancreas is almost always of the spheroidal-cell type. It is liable to undergo softening in the centre, and sometimes it undergoes the colloid change. It tends to form secondary deposits in the neighbourhood, particularly in the lymphatic glands at the hilum of the liver, but it is less likely to form secondary growths in the liver itself than many other forms of carcinoma, notably those of the stomach and the intestine.

The pancreas is sometimes the seat of **cysts**. In some cases these cysts are dilated portions of the pancreatic duct or its tributaries. That the pancreatic duct itself sometimes undergoes dilatation, we have ample evidence in those cases in which there is an obstruction at the orifice of the combined pancreatic and hepatic ducts on the papilla in the duodenum, and in cases in which the main duct is obstructed by a pancreatic calculus. Sometimes the cysts reach to a considerable size. They are, however, of rare occurrence.

Concretions are sometimes found in the pancreatic duct. They are usually less in size than a hazel nut, are round or oval, and of a white or greyish colour. As a rule, they are present in dilated ducts, and it is probable that they are the cause of the dilatation. They are generally composed of calcium carbonate and phosphate.

SECTION XII

THE RESPIRATORY ORGANS

(1) THE LARYNX AND TRACHEA

The pathological conditions which affect the larynx and trachea are not numerous, but in the case of the larynx especially, owing to the narrowness of the glottis, the importance of such conditions as obtain is considerable.

Calcification of the laryngeal cartilages is almost a constant accompaniment of advancing years. The thyroid and cricoid cartilages in particular are very liable to be infiltrated to so considerable an extent that it is difficult to divide them with the scissors. True ossification of the cartilages also occurs, but is less common. When it is present the bone formed is of a somewhat cancellous type.

In the trachea an irregular deposition of calcium salts is sometimes seen. This deposition is always on the anterior aspect of the tube, and generally extends over several cartilaginous rings on the internal surface immediately beneath the mucous membrane. It is arranged longitudinally to the trachea, and apparently has some analogies with the calcification which occurs in atheromatous patches in the great arteries. So far as is known the condition is without clinical significance.

Inflammation affects the larynx both in the acute and in the chronic forms. Moreover we meet with simple as well as with special varieties of inflammation. Of these short descriptions must be given.

(1) **Acute laryngitis** is generally the result of exposure to cold or depends upon the inhalation of irritating vapours. In either case the appearances are the same. They consist in an intense redness of the mucous membrane of the larynx with swelling, and frequently the presence of a thick mucous discharge in the later stages and a thin watery discharge in the earlier. The entire mucous membrane of the larynx is affected, but the

parts that show the greatest changes are the vocal cords. These are of a raw beef colour instead of a glistening white, and instead of being smooth and shiny are dull and granular. The amount of swelling is not confined to the cords, but is to be recognised in their entire neighbourhood. Upwards we may find that the pharynx is acutely inflamed.

(2) In **chronic laryngitis** the changes are very similar, only not so intense. On the other hand, we find that the swelling of the parts is not due to the presence of an increase in the amount of fluid in the soft tissues so much as to the existence of an increased amount of fibrous tissue. This is particularly noticeable in the case of the vocal cords, which are thickened, stiff, and have irregular margins. They may be of a fairly normal colour, but it is commoner to find that they are reddened.

A slight degree of chronic laryngitis which is very liable to undergo exacerbations constitutes the condition known as 'clergyman's throat.' It arises from excessive use of the voice.

A condition of the larynx which has close analogies with laryngitis is acute **œdema**. This change may come on in the course of an acute or a chronic laryngitis, and then it is certainly of an inflammatory nature. But it may also appear in the course of acute nephritis, and then it has more in common with the general dropsy that characterises this disease, and must not be looked upon as inflammatory. In either case the condition shows itself by the production of an intense œdema of the mucous and submucous tissue bordering on and lining the glottis. As the consequence of this œdema the rima glottidis is markedly encroached upon and the dangers of suffocation are considerable. When viewed with the laryngoscope, the affected part may be red in colour, but more commonly it is pale from the anæmia which is induced by the pressure on the vessels of the exuded fluid. The epiglottis may be so considerably swollen that it is readily felt by passing the finger to the back of the tongue.

Inflammatory conditions of the kind that have been mentioned may also arise as the result of swallowing corrosive fluids, but there is nothing special in this point to call for remark.

(3) **Ulceration** of the mucous membrane of the larynx is not a characteristic of the forms of inflammation just described, but in the greater number of inflammatory affections of the part ulceration is a more or less pronounced feature.

(*a*) In **diphtheria** the amount of ulceration that occurs when the larynx is affected is generally slight. It is none the less certain, and the membrane is attached to the deeper layers of the mucous membrane. The 'false membrane,' in fact, largely consists of the necrosed superficial portions of the mucous membrane. In addition to the presence of membrane in the rima itself, the softer tissues around are largely infiltrated with the products of inflammation, and as a result the interference with the freedom of respiration is considerable. To the subject of diphtheria generally we have already given sufficient attention.

Apart from the ulceration which accompanies malignant disease of the larynx—and to this attention will be turned later—the most important varieties of laryngeal ulceration are those which are associated with tuberculosis and syphilis.

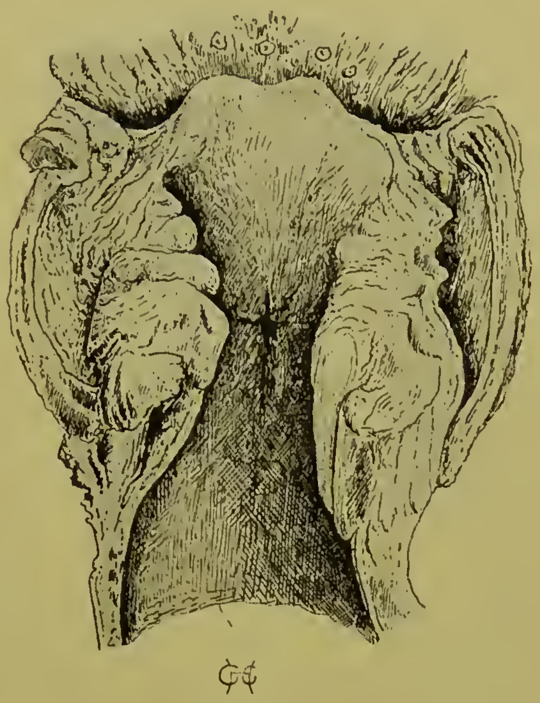


Fig. 111.—Tuberculous Disease of Larynx. Natural Size.

Opened and seen from behind. The arytæno-epiglottidean folds are enormously thickened, but there is no obvious ulceration.

(*b*) **Tuberculosis** shows itself both by the presence of an inflammatory thickening of the soft parts about the larynx and by a definite ulceration which may affect both the soft and the hard parts, such as the vocal cords themselves. The situation which is liable to be first attacked and the one which generally, therefore, shows the most marked evidences of disease, is the arytæno-epiglottidean fold on either side. In addition, one finds the false cords thickened, and the true cords may also be affected in the later stages of the condition. At first the change consists in chronic inflammatory thickening alone, but when the disease has lasted some time ulceration makes its appearance. It generally occurs within the glottis, and leads to destruction of the true and false cords and the mucous membrane in their neighbourhood over a larger or smaller area. The altered tissue may be reddish in colour, but generally it is pale pink or even definitely anæmic. The ulceration also affects the base and edges of the epiglottis, and may extend to the tip of the epiglottis and the base of the tongue. Histologically, it has the ordinary characters of tuberculous material.

Tuberculous disease of the larynx is perhaps never found apart from tuberculosis of the lungs. It is believed that the condition is the result of direct infection of the larynx by the tuberculous sputum. From this point of view it is intelligible that the two sides of the larynx are liable to be affected fairly equally in any case. The amount of stenosis that is produced as the combined result of the actual tuberculosis and the superadded inflammation due to simple irritation is sometimes such that tracheotomy is necessary.

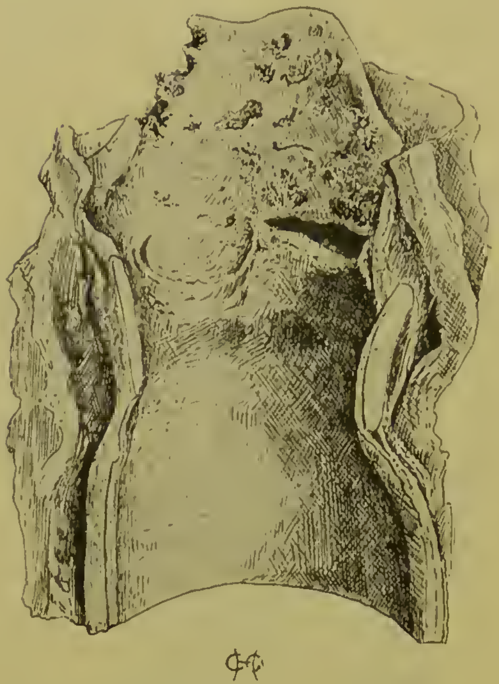


FIG. 112.—SYPHILITIC ULCERATION OF LARYNX. NATURAL SIZE.

The left upper margin of the epiglottis and the left true and false vocal cords have disappeared, while numerous shallow ulcers are visible on the under surface of the epiglottis. The edges of the right true and false vocal cords are much thickened.

(*c*) **Syphilis** affects the larynx as a late secondary or an early tertiary phenomenon. Hence the characters of the inflammation vary in different cases. In some the change consists in the formation of papillomatous overgrowths of the mucous membrane similar to those which constitute 'mucous tubercles' and condylomata. These may be found anywhere on the mucous membrane of the larynx or its neighbourhood. But far more common and characteristic are definite inflammatory thickenings and gummatous formations which go on to ulceration and subsequently to the formation of fibrous tissue. One of the chief situations of these changes is the tip of the epiglottis; in time the entire epiglottis may be destroyed. The infiltrations and ulcerations extend more widely, however, and a great part of the entire laryngeal mucous membrane is liable to be affected. The inflammation may also extend to the perichondrium and lead to necrosis of the cartilages. Hence the total amount of destruction that may result from syphilitic inflammation of the larynx is very considerable. With the onset of repair fibrous tissue is formed as in other cases, and the final deformity of the larynx may be extreme.

(*d*) In **leprosy** the larynx may be affected by the same process that is seen in the skin and the nerves, or it may be affected by a truly tuberculous change concomitant with the pulmonary tuberculosis to which leprous patients are liable. In the latter case there is nothing to call for further remark, but when the larynx is affected by true leprosy the first appearance is a nodular one involving the mucous and submucous coverings of the part. The nodules undergo ulceration, and then the amount of destruction of the larynx, including its cartilages, may be very great. There is not nearly the same tendency to the formation of fibrous tissue that there is in the case of syphilis.

(*e*) Several of the acute specific fevers are apt to be accompanied by the formation of small ulcers in the larynx and the trachea. Thus they may be seen in cases of **variola**. But a more important cause of this condition is typhoid fever, owing to the greater frequency of the disease in this country. The formation of these ulcers is associated with an acute inflammation of the laryngeal mucous membrane, and the amount of swelling may be severe. In certain of the other exanthemata (e.g. scarlatina) we may find a somewhat similar condition, but in them the loss of substance consists rather in erosion than in ulceration.

In **typhoid** fever when inflammation of the larynx occurs, it almost always goes on to perichondritis and necrosis of some of the cartilages. The arytænoid cartilages are thus liable to be affected, and they may be found lying loose in a mass of necrotic tissue at the autopsy. The degree to which the larynx is affected in typhoid fever varies somewhat, but it is rarely so widespread as in the other conditions which we have considered. It may be, however, that a portion of the epiglottis undergoes necrosis as well as the arytænoid cartilages. This complication of typhoid fever is not a very common one.

Ulcerative conditions of the trachea are not common or important. As a rule, they are associated with a similar change in the larynx or in the bronchi. Thus in severe tuberculous affection of the larynx we are liable to find a certain number of ulcers in the trachea also, and the same is true for variola. The most important form of ulceration of the trachea is that which depends upon pressure atrophy induced by a mass outside the trachea. Thus a communication may be established between the œsophagus and the trachea in cases of malignant disease of the œsophagus, or an aneurysm may ulcerate and burst into the trachea. But it is commoner, if such ulceration occurs, for it to take place into one of the bronchi than into the trachea itself.

Inflammation of the trachea (**tracheitis**) apart from the ulceration is an unimportant although a painful affection. It occurs whenever the trachea has been exposed to the effect of irritating vapours, and accompanies the onset of a large proportion of ordinary coryzal attacks. The mucous membrane of the trachea under these conditions is red, dry, and swollen at first, but later it becomes covered with a fairly thick layer of mucus. When the trachea has been long affected by a chronic inflammation, as in cases of chronic bronchitis, the mucous membrane may be largely destroyed, leaving a denuded muscular layer exposed.

As the result of pressure from without, both the larynx and the trachea may become altered in shape and position. Of the two parts the trachea is the more liable to be affected, and sometimes it is flattened to so considerable an extent that its walls are almost in contact. At the same time it may be pushed far over to one side or other of the neck. Changes of this kind are especially seen in cases of lymphadenoma and lympho-sarcoma, owing to the pressure exerted by the masses of enlarged glands, and in goitre.

The larynx is less liable to be directly affected by pressure than the trachea, but it undergoes important modifications in shape when some cause exists which leads to paralysis of the laryngeal muscles. Here the change does not so much affect the general shape of the part as the shape of the rima glottidis. With complete **abductor paralysis**, for example, which occurs in cases of disease of the bulb, the glottic opening may be reduced to a mere chink. In **laryngismus stridulus** a similar closure of the glottis occurs, but it is of a spasmodic nature, and is accompanied, so far as is known, by no anatomical changes beyond the general existence of rickets, with which the condition is closely bound up.

(4) **New-growths.**—New growths of the trachea may be very shortly dismissed. They only occur as the secondary result of the extension of a growth from some neighbouring part, such as the œsophagus, and even then they are not very common.

Malignant disease of the larynx forms the most important of the new-growths of the parts under consideration, but in addition to malignant growths, non-malignant growths, in the form of papillomata, are known to occur. In papilloma the tumour is built up of a material which is usually covered by squamous epithelium, and in carcinoma the same variety of epithelium is generally present. This is only natural when we remember that the squamous epithelium of the mouth is continued down as far as the vocal cords.

(*a*) Papilloma of the larynx is the commonest form of new-growth of the part. It frequently arises subsequently to repeated attacks of laryngitis, and most generally springs from the vocal cords. The pedicle of attachment may be broad, and then the papilloma has somewhat of a cauliflower appearance, or it may be narrow and long, and then the growth is more or less filiform. The amount of epithelium which covers the fibrous-tissue structure of the growth varies considerably, but usually there is a somewhat thick layer. It is generally squamous, but may be columnar.

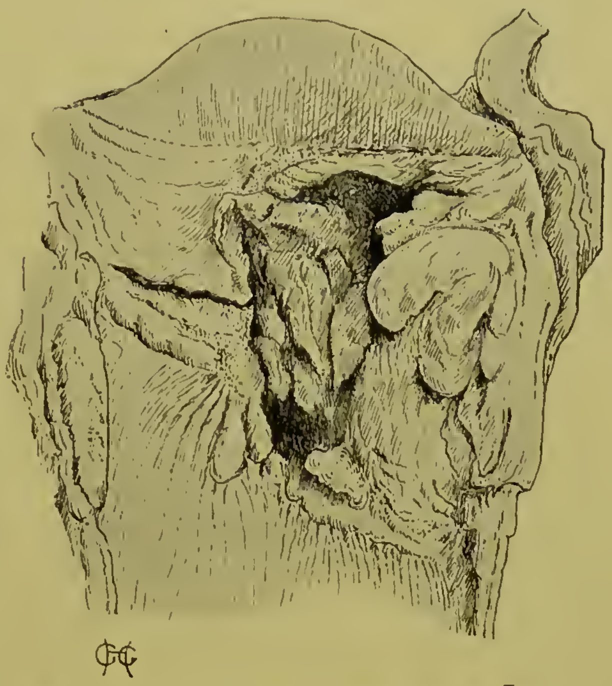


FIG. 113.—MALIGNANT ULCERATION OF LARYNX. NATURAL SIZE.

The right half of the larynx is replaced by an irregular ulcer with thick everted edges. The condition has extended for a short distance down the trachea.

Carcinoma of the larynx commences as a small growth which has many resemblances to a warty papilloma. Its base is broad and its surface is irregular. It increases in size with fair rapidity, and ultimately the amount of tissue which it destroys is considerable. It usually arises from one of the vocal cords and leads to a destruction of tissue which is more marked on one side of the larynx, in this point offering some contrast to the destruction which accompanies syphilis and tuberculosis. It extends in all directions, and whereas it is rare for syphilis or tuberculosis to affect the thyroid cartilage, it is not very rare for this to happen in cases of carcinoma. If it arises from parts above the vocal cords, the growth is of the squamous-cell variety; if from parts below, it is columnar cell.

In addition to the growths which have been mentioned above, the larynx may be the seat of ordinary fibromata and occasionally of sarcomata. Fibromata are the least uncommon of the rarer forms of growth.

(2) THE BRONCHIAL TUBES

Practically the only morbid conditions of the bronchi are those which consist in inflammation and the results of inflammation. This inflammation may primarily concern the bronchi, or it may primarily affect the pulmonary tissue and induce bronchial changes secondarily.

(1) **Acute inflammation.**—The bronchi are liable to be affected by acute inflammation throughout their entire course, but it is far commoner for the change to be seen in the case of the finer tubes than in those of the first and second order of magnitude. In this respect there is a marked contrast between acute and chronic bronchitis. A further point of difference lies in the fact that, whereas chronic bronchitis is one of the commonest morbid conditions, acute bronchitis is rare. From the fact that it is the smaller tubes that are affected, it is customary with some authors to designate the condition by the name acute 'bronchiolitis.' This is, no doubt, the most common situation of the acute inflammation, but it must not be forgotten that the large bronchi are sometimes affected with an inflammation of the acutest kind—for example, when an intensely irritating vapour has been inhaled. Whether it be the large or the small bronchi that are affected, the appearances of the tubes are the same. They are of a brilliant red colour, swollen, sometimes dry, sometimes moist, with a copious watery exudation, and the inflammation, although it principally affects the mucous membrane, is obviously present throughout the entire thickness of the bronchial tube.

When the smaller tubes within the lungs are affected, the inflammation extends to the pulmonary tissue in the midst of which the bronchi are situated. In these cases, therefore, true pulmonary changes are superadded upon the bronchial. We shall not here stop to consider them, but it may be mentioned that the pulmonary changes consist in the production of a broncho-pneumonia.

Microscopically, the changes are those of an intense inflammation, the destructive phenomena being particularly noticeable. The epithelial lining of the tubes shows signs of proliferation and desquamation. Frequently the entire lining of the tubule lies detached in the lumen along with exudation fluid and a greater or smaller number of migrated leucocytes. The muscular coat is infiltrated with small round cells, and the muscle cells are granular in appearance. In the peribronchial tissue there are evidences of great congestion in the numerous dilated blood-vessels that are present. In the case of the larger tubes these peripheral changes are not so evident, but the inflammation expends itself principally upon the mucous membrane and the submucous tissue. Here the changes are similar to those which have been described.

(2) **Chronic inflammation.** — (*a*) **Chronic bronchitis** affects bronchi of larger size, and the changes to which it gives rise are very characteristic. The most important of them is a loss of the mucous membrane entirely, so that the muscular coat becomes clearly visible. Lying between the individual bands of muscular tissue are small pits where the inflammation has extended to the deeper parts. The inner lining of the tubes is redder than normal, and they are moist with a watery fluid that escapes from the denuded surfaces. Similar appearances are met with in no other condition than chronic bronchitis. The change is generally present in the trachea as well as in the large bronchi in any case that is of sŏme standing. Chronic bronchitis is usually associated with a greater or less amount of pulmonary emphysema.

(*b*) **Peribronchitis** is usually present to some extent in all pulmonary diseases of a chronic nature. Occasionally, however, it is very pronounced. In these cases the bronchi are seen to be surrounded by an irregular mass of dense fibrous tissue which there is no doubt, from its general appearance, is of inflammatory origin. It is the smaller bronchi that are affected in this way rather than the larger. As to the origin of the condition it is difficult to speak with certainty. In some cases it is associated with pulmonary tuberculosis of a more or less chronic kind, and then we may perhaps assume that the irritant has been inhaled and, passing through the mucous coat, first leads to inflammation in the peribronchial tissue.

(*c*) **Plastic bronchitis** is a disease which is very characteristic clinically, but concerning the pathology of which we are very ignorant. In it the patient expectorates a complete fibrinous cast of some portion of the bronchial tree. This may occur time after time. We cannot but conclude that the cast has been formed in the bronchi, that it consists of fibrin which has formed from an exudation in the region at which it was formed, and the case of diphtheria naturally rises to our mind. More than this cannot be said, for cases are so rare that the opportunities for pathological investigation are very limited.

(*d*) **Syphilis.**—Tuberculous affections of the bronchi may be left until we come to consider tuberculosis of the lungs generally, but syphilis produces one change that is so definitely localised in the bronchi that it must be mentioned separately.

The change consists in the production of an ulceration followed by stenotic cicatrisation of the right or left bronchus, or perhaps of both. The cases in which the actual ulceration is seen are uncommon ; it is far more usual to find that there is, at the very commencement of the bronchus, a definite ridge or circular mass of dense fibrous tissue which reduces the diameter of the lumen to a considerable extent.

There is some uncertainty as to the actual situation in which the ulceration commences. That is to say, it is doubtful whether it commences in the mucous membrane of the bronchus, or whether it commences in the lymphatic glands that lie beneath the tracheal bifurcation and extends from them into the bronchus. Cases can be shown which support either view, but the fact that we sometimes see examples of a syphilitic ulceration of the mucous membrane of the bronchus in the very situation in which it is customary for stenosis to be present, unassociated with any alteration of the infra-tracheal glands, is strong argument that the condition primarily affects the bronchus itself. Microscopically, the change manifests no particular characters.

(3) **Bronchiectasis.**—Although the conditions which are associated with bronchiectasis are essentially pulmonary as distinguished from bronchial, the change itself is one so characteristic of the bronchi that it is convenient to mention it here. The change consists in a dilatation of the whole or some part of the bronchial tree. The smaller bronchi at the peripheral portions of the lung are the most commonly affected, and those serving the lower lobe are dilated more often than those of the upper. The dilatation itself may be either fusiform or saccular, and of these two varieties the saccular is the more common. The cavities thus formed are sometimes of considerable size ; in a few instances they may be as large as a Tangerine orange. As a rule, however, they are not larger than filberts, but then they are likely to make up by their numbers for their lack of individual size.

When a lung which is the seat of bronchiectasis is cut into, there appear a number of cavities containing a purulent fluid. When this fluid has been washed away the appearance of the cut section is much that of Gruyère cheese. At some point in the wall of the cavity, which is quite smooth on its internal surface, it is seen that the cavity communicates with a bronchus, and if the pulmonary tissue proper is removed by maceration or other means, the bronchi are seen to be the seat of a number of sacculi arranged in moniliform fashion. Around the bronchiectatic cavities there is always a considerable increase in the amount of fibrous tissue in the lung generally, which has been produced as the result of a long-continued inflammation of chronic type. It is owing to the contraction of this fibrous tissue that the bronchiectases are formed; at one place it exerts traction upon the walls of the bronchi, and at another it constricts the lumina of the tubes.

The condition may be confused with that in which there is basal tuberculosis of the lung with the formation of cavities, but the smooth nature of the walls, the multiplicity of the cavities, and their definite connection with the bronchi, a point which can always be made out with a little care, are sufficient to effect a diagnosis.

So far as the actual nature of the changes which take place in the bronchial walls are concerned, it is possible to distinguish an atrophic from a hypertrophic variety of bronchiectasis. In the atrophic variety, which is the commonest, the condition is brought about by a gradual weakening of the bronchial coats by a long-continued inflammation. In these cases the mucous membrane is generally more or less atrophied and infiltrated with cells, but the epithelial layer itself may be well preserved, though the cells are frequently found to be flattened rather than columnar. In hypertrophic bronchiectasis the changes in the mucous membrane are similar to those in the atrophic form, but the firmer portions of the wall become thickened with added fibrous tissue. This variety occurs particularly under conditions in which a large portion of the pulmonary tissue surrounding the bronchi is deprived of its function: as a consequence the air which enters the bronchi exerts its pressure rather upon them than upon the lung tissue as is normally the case.

(3) THE LUNGS

The morbid changes which are undergone by the lungs are of the most different descriptions. Malformations we may leave entirely on one side, for they are of little clinical importance, although, so far as the variations are concerned to which the individual lobes are divided, minor malformations are not infrequent.

(1) **Atelectasis.**—In the fœtus the lungs are, of course, quite unexpanded, and after birth this condition may persist to a certain extent. This pathological condition, which is known as

atelectasis, is only seen in weakly infants, although it is possible that the absence of function may lead to alterations that persist as anatomical variations into later life. The lung in atelectasis may be affected in its entirety, or a lobe may be affected, or the condition may involve only a portion of a lobe. In any case the affected portion is completely airless, and as a consequence the walls of the alveoli are practically in contact. The blood-vessels are of small size and contain but a small quantity of blood.

The airless condition of the lung which has just been mentioned has somewhat different appearances, both macroscopically and microscopically, from the airless condition which is of frequent occurrence under a variety of circumstances in lungs that, at birth, were normally expanded. These differences partly depend upon the alteration which is induced in the capacity of the pulmonary vessels with the expansion of the lung, and partly upon the fact that we meet with an airless condition of this kind only in association with other morbid changes which are liable to be either inflammatory or productive of inflammation. Owing to these differences it is customary to reserve for the condition a particular name, and speak of it as **collapse**, or, under special circumstances, as **carnification**.

(2) **Collapse of lung** is the result of the removal of air from vesicles that were formerly expanded. The walls of the alveoli are therefore brought into contact as in atelectasis, but not to quite the same extent. For the altered conditions of the pulmonary tissue act upon it in the light of an irritant and induce a certain amount of inflammation. Hence the blood-vessels become expanded and more obvious than normal, there takes place a certain migration of leucocytes that pass into the potential alveolar space, and this is conjoined with a small exudation of fluid. The portion of lung tissue, therefore, is more voluminous than is a corresponding portion of atelectatic lung, and is at the same time altered by a low form of inflammation.

Collapsed lung is generally easily recognisable by its smaller bulk, by its far darker colour, and by the fact that it sinks in water. When the foci of collapse are scattered throughout a lobe or the whole of a lung, they are seen to be situated on a lower level than the expanded portions that lie in their immediate proximity. This contrast is the more marked in that, as will be seen later, there is a tendency for lung tissue in the immediate neighbourhood of a patch of collapse to undergo a hyperdistension.

The two conditions under which collapse of lung is most liable to occur are *broncho-pneumonia* and *pleural effusion.* Although the main histological features of the altered tissue are the same in both cases, the macroscopic pictures are somewhat different. In association with broncho-pneumonia the patches of collapse are generally distributed with fair evenness throughout the two lungs, although the lower lobes on both sides are more liable to suffer. At the same time the individual patches are irregular in shape, and, as a rule, small, though considerable tracts of lung may be rendered functionless by the union of neighbouring patches of collapse. The depressed nature and the deep purple colour of the foci are, in addition, noticeable characters of the collapse that accompanies broncho-pneumonia. In cases where there is a pleural effusion, on the other hand, it is customary to find that a tract of pulmonary tissue has undergone collapse, whether it be only a small portion at the base of the lower lobe (the amount of effusion being small), or an entire lower lobe, or the whole lung (the effusion being more voluminous). Not only, therefore, is the mass of collapsed tissue larger in these cases, but it is also less interspersed with normal air-containing lung tissue. Moreover it is not so easy to distinguish the depressed nature of the patch in many cases, owing to the fact that the collapsed lung rather shades off imperceptibly into the normal than shows a sharp transition. Although inflammatory changes undoubtedly occur in lung which has undergone collapse, owing to the presence of a pleural effusion, they are rarely so pronounced as in cases which are associated with broncho-pneumonia.

For the production of collapse it is not necessary that the pleural cavity should become filled, or partially filled, with liquid. Air, as in the production of a pneumothorax, or a solid growth, is equally effective. In both of these cases, however, a short time only is necessary for the primary condition to be complicated by the outpouring of fluid. In the case of a solid growth which involves the pleura, the fluid is generally serous, perhaps mixed with a certain amount of blood; in the case of a pneumothorax it is probably pus. Under either circumstance a portion or the whole of the lung becomes the seat of collapse.

If the collapsed condition of the lung does not persist too long, it is possible for the alveoli to again expand on removal of the cause which determined their collapse. Thus, evacuation of a pleural effusion, or recovery from a broncho-pneumonia, is after a short interval followed by a return of the normal function. But this is only possible if the collapsed condition has not been too protracted. If this be the case, the lung remains airless and is then said to have passed into a condition of carnification.

(3) **Carnification** of lung is especially seen in cases in which the collapse has been brought about by the presence of a collection of fluid in the pleural cavity, whatever the cause of that collection may have been. The entire lung is then frequently affected, and lies at the back of the pleural cavity close to the spinal column. On auscultation it is found that no air enters into it at all. The macroscopic characters of carnified lung are very similar to those of collapsed lung, but the mass of tissue is tougher and browner in colour from the greater amount of fibrous tissue which it contains, and the presence in it of a certain amount of pigment derived from the breaking down of blood corpuscles. Under the microscope it is seen that the signs of active inflammation are less marked than in the case of collapse.

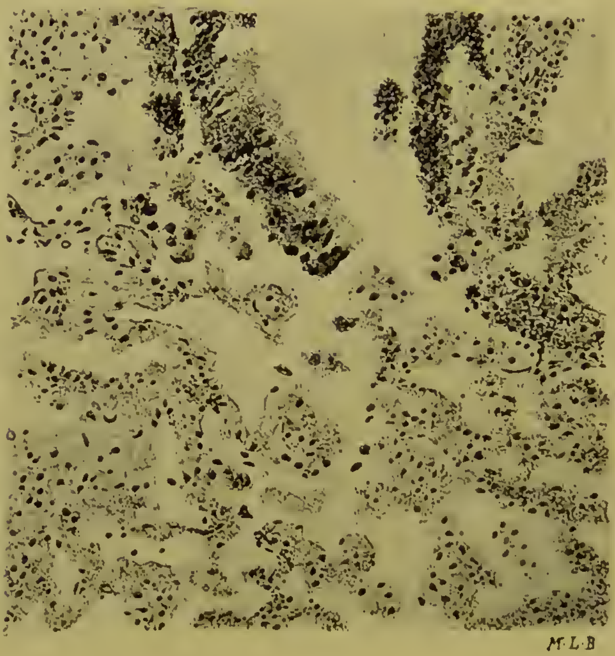


Fig. 114.—Section of Carnified Lung. × 420.

The alveolar walls are thickened and infiltrated with leucocytes, while there is a certain amount of proliferation of their lining endothelial cells. The normal air-containing space of the alveolus is almost obliterated. The bronchiole (above) shows the existence of broncho-pneumonia by proliferation of the cells of the lining membrane.

(4) **Emphysema.**—Emphysema is essentially an atrophic condition of the walls of the air vesicles in consequence of which they yield to the pressure of the air within them. This yielding is especially apt to occur when the intra-pulmonary pressure is increased above the normal, and therefore emphysema is seen most commonly in connection with diseases in which cough is

a prominent symptom and in persons whose occupation leads them to confine the air within the lungs under pressure (e.g. cornet players). This mechanical cause is not, however, the entire explanation, for we meet with emphysema in young children occasionally where the factors mentioned are not in action. Nevertheless such young children are generally the subjects of asthma, a condition in which the lumen of the smaller bronchioles is constricted either by a spasm of the muscular tissue which enters largely into the composition of their walls, or by a sudden congestion and swelling of the bronchial mucous membrane, or by both factors combined. It is practically certain, however, that there comes into play, in addition, an hereditary deficient elasticity of the pulmonary tissue which interferes with the proper return to the normal at the end of expiration.

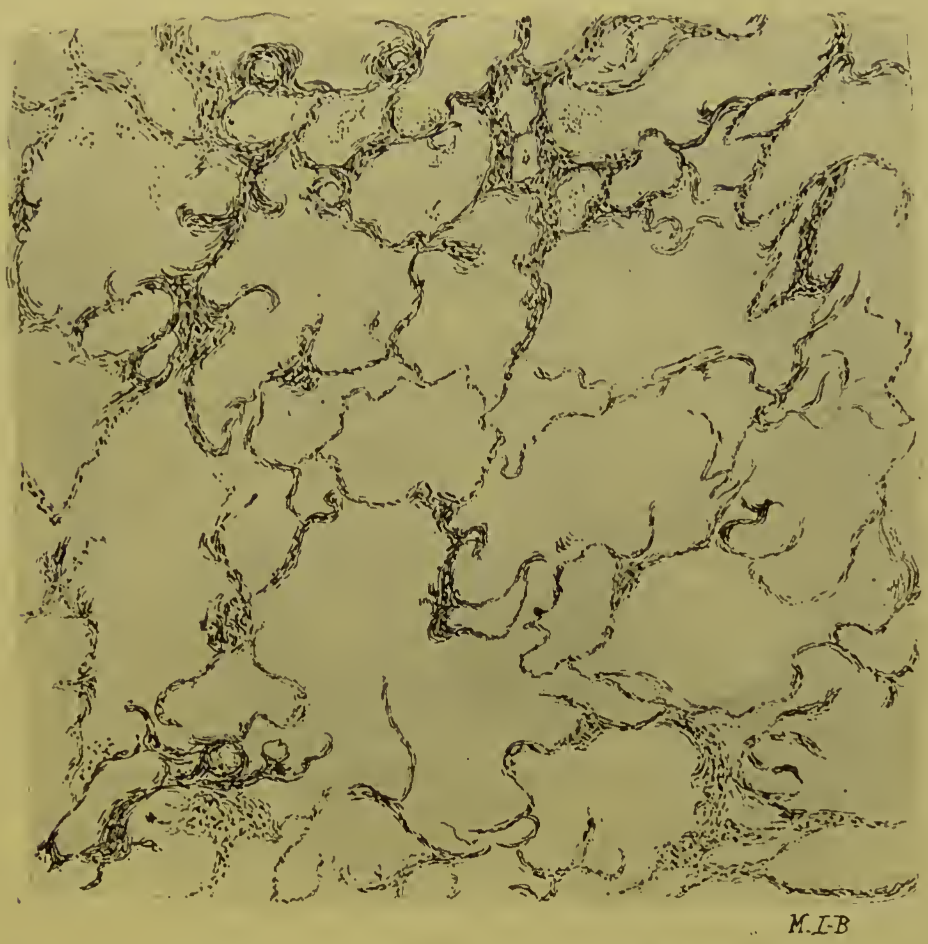


Fig. 115.—Section of Lung showing Vesicular Emphysema. × 60.

Along the upper margin of the figure the lung tissue is fairly normal, but elsewhere the air spaces are large owing to rupture of several alveoli into one (cf. right upper corner). The alveolar wall in the emphysematous portion is thin and the nuclei of very few cells are seen. In many places the free ends of ruptured alveolar walls are present.

It is customary to distinguish certain varieties of emphysema. Thus we have the **vesicular**, in which the change affects the air vesicles and is generally fairly evenly distributed throughout the lung; the **lobular**, in which the change is of a larger size and in which the foci affected are more discrete and more obvious to the naked eye; and the **bullous**, in which the change is accompanied by the formation of distinct blebs that often reach to a considerable size and may affect a very large portion of an entire lobe.

In all the varieties of emphysema the essential condition is the same; the differences only depend upon the degree to which the change has been carried. On examining a microscopic section, it is seen that the alveolar walls are thinner than normal, that the capillary vessels running in the walls are stretched and their lumina are narrowed, that the endothelial cells lining the alveoli are even flatter and less distinct than normal, and that in many places the boundary walls between adjacent alveoli have given way so that several alveoli are converted into one large cavity. It is the degree to which this latter process has proceeded that determines in large measure the macroscopic character of the variety of emphysema present.

Although we may find that the entire lung is modified in the directions that have been indicated, we always find that the emphysema is more marked in some situations than in others. It is in the least supported regions that the greatest effect of the increased intra-pulmonary pressure manifests itself, and hence it is especially the supra-clavicular portions of the upper lobes and the anterior margins of the various lobes that are the principal seats of emphysema.

Owing to the fact that cough is a highly potent factor in inducing emphysema, the condition frequently follows upon, and is almost always associated with, chronic bronchitis.

A somewhat special variety of emphysema is known which is termed **compensatory.** It is found immediately around a mass of consolidated or collapsed lung. It is in part to the presence of this surrounding area of emphysema that the depressed appearance of a focus of collapse is due. The actual changes in these areas of compensatory emphysema are the same as those in ordinary vesicular forms.

(5) **Non-inflammatory vascular changes.**—The principal non-inflammatory vascular changes affecting the lungs are associated with cardiac diseases of different kinds, though they may occur under other conditions.

(*a*) **Congestion and brown induration.**—These conditions are to be regarded somewhat in the light of cause and effect. They are seen in cases in which there is an interference in the passage of blood through the capillaries of the lungs, owing to some fault in the heart, whether that cardiac fault is primary or is secondary to some other condition (e.g. chronic renal fibrosis.) Under any circumstances the capillaries of the lungs, which are normally wider than any others in the body, become markedly dilated and engorged with blood. When the heart's action is very weak, the congestion is definitely localised to a greater extent in the posterior parts of the lungs and constitutes **hypostatic congestion.**

This condition is liable to pass gradually into a low form of inflammation known as **hypostatic pneumonia.**

In ordinary congestion of the lungs the microscopical appearances are consistent with the vascular alterations which have been described. The alveolar walls are wider than normal, owing to the presence in them of the dilated capillaries. In severe cases it is found that there has taken place an exudation of fluid into the air vesicles, and sometimes small numbers of red blood corpuscles are present as well. The presence of fluid leading to œdema of the lung is more common in this variety of congestion than the presence of red blood corpuscles.

In hypostatic congestion the blood-vessels are far more engorged than they are in the ordinary form of congestion. At the same time there is an exudation of fluid into the alveolar spaces and a much greater tendency for the escape of red corpuscles from the vessels in the alveolar spaces. To so considerable an extent does this filling of the air spaces go, that it is often difficult to determine whether any air is left in the affected portion of lung at all. Under these conditions we have a state that borders upon a definitely inflammatory pneumonia. A further point of resemblance lies in the fact that there sometimes occurs a coagulation of the exuded fluid, with the production of strands of fibrin similar to that which is one of the most characteristic features of pneumonia.

When congestion has lasted for a considerable time in the lungs, it leads to the existence of a permanent alteration in their colour and consistency. This brown induration is the combined result of the presence of a large amount of brown pigment similar to that which is found in nutmeg liver, and is derived from the red blood corpuscles that undergo degeneration in the lung, together with an increase in the amount of fibrous tissue present, not only in the fibrous septa of the lung, but also in the walls of the alveoli themselves. By the time that brown induration has become fully established the evidences of congestion have largely disappeared by a process of automatic extinction.

(*b*) **Œdema.**—Under a variety of conditions there occurs an output of œdema fluid into the air sacs. The conditions under which this takes place are practically identical with those which lead to congestion, and therefore congestion and œdema are generally found in conjunction. The fluid itself is of a watery consistency, and is colourless in the majority of cases, though it may be pink or red from an admixture of red blood corpuscles or dissolved hæmoglobin. The amount that is poured out varies considerably. In most instances a certain amount of air still remains in the air vesicles, but sometimes the affected portion of lung becomes completely solidified with the fluid and sinks in water. Macroscopically, in addition to the characters that have been noted, an œdematous lung is more voluminous than normal; microscopically, the alterations are but slight, and consist principally in the existence of a small quantity of precipitated albumin in the air vesicles.

(*c*) **Intra-alveolar hæmorrhages.**—Under this name are included two conditions which have many points in common, but which are nevertheless intrinsically different. These two conditions are **hæmorrhagic infarction** and **pulmonary apoplexy**.

In both conditions we find that the lung shows at some point on its periphery, and particularly at the margin of a lobe, a solid mass which projects somewhat beyond the general level of the rest of the organ, which is more or less wedge-shaped on section, and which has a colour resembling that of black currant jelly. Microscopic examination shows that the alveoli in the affected area are everywhere filled to their utmost capacity with red blood corpuscles.

Although the picture is the same, it is probable that two distinct conditions may be concerned in its production. Owing to the arrangement of the terminal bronchi and the terminal branches of the pulmonary artery, it is clear that a wedge-shaped area (on section) will be produced either if blood becomes effused into a terminal bronchus and passes down to the infundibulum and air sacs, or if blood becomes extravasated from the terminal capillaries of a branch of the pulmonary artery into the air sacs with which they are in immediate relation. The former condition will obtain if blood is extravasated into a bronchus, the latter if an embolus becomes lodged in a terminal branch of the pulmonary artery. There is a difference of opinion as to the relative frequency with which these two contingencies happen.

It may be mentioned here that we occasionally meet with cases in which the embolus is not fibrin, but either a fat globule or a small quantity of air. **Fat embolism** occurs in cases in which there has been an extensive fracture of bone, with the consequent setting free of some of the fat of the medulla into the circulation. So far as the results which follow the embolism are concerned, they are similar to those met with in other cases, but it is, of course, possible to determine the nature of the embolus by staining with osmic acid. **Air embolism** occurs when air has been drawn into a large vein close to the thorax, owing to an opening in the wall. It is of very rare occurrence, and does not call for special notice. Anæmic infarcts of the lung occur, but are uncommon.

(6) **Inflammation and its sequels.**—These form by far the most important morbid affections of the lungs. They may be acute or chronic, and the sequels may be pathological or physiological.

(*a*) **Lobar pueumonia.**—This condition, as its name implies, affects entire lobes of the lung. It is also called *croupous* pneumonia from the main appearances of the inflammation, but the name is a bad one, because we sometimes meet with forms of inflammation of the lung which have very similar microscopic appearances, but differ from lobar pneumonia in point of their ætiology.

In lobar pneumonia one or more entire lobes of one or of both lungs are found to have undergone change. In most instances when the patient dies it is found that the affected part is no longer spongy but has become completely consolidated. So marked is this change that the altered lung has been likened to liver substance, and the condition has received the name of 'hepatisation.' Such altered lung sinks at once if placed in water. At the same time its colour is altered. As a rule it is greyish, but it may be midway in colour between a red and a grey. Far less commonly it is of a deep red colour. Occasionally we find that while the main portion of the affected lung is grey, there is a portion, perhaps, in another lobe, or even in the other lung, which is red, but it is usual to find that all the affected lung has a more or less uniform colour. The affected lobe is far bulkier and heavier than normal. The bulkiness is shown by the degree to which the visceral pleura is stretched over the surface, and the weight may be greater by a couple of pounds than that of an unaffected corresponding lobe. It is invariable to find small or great evidences of a recent pleurisy over the inflamed lobe.

When a portion of such a lung is examined histologically, it is found that its appearances differ according to the length of time that has elapsed between the onset of the disease and the death of the patient. Clinically it is customary to divide acute lobar pneumonia into stages. Thus we speak of a stage of congestion, one of red hepatisation, and one of grey hepatisation; these constitute the truly inflammatory portions of the disease.

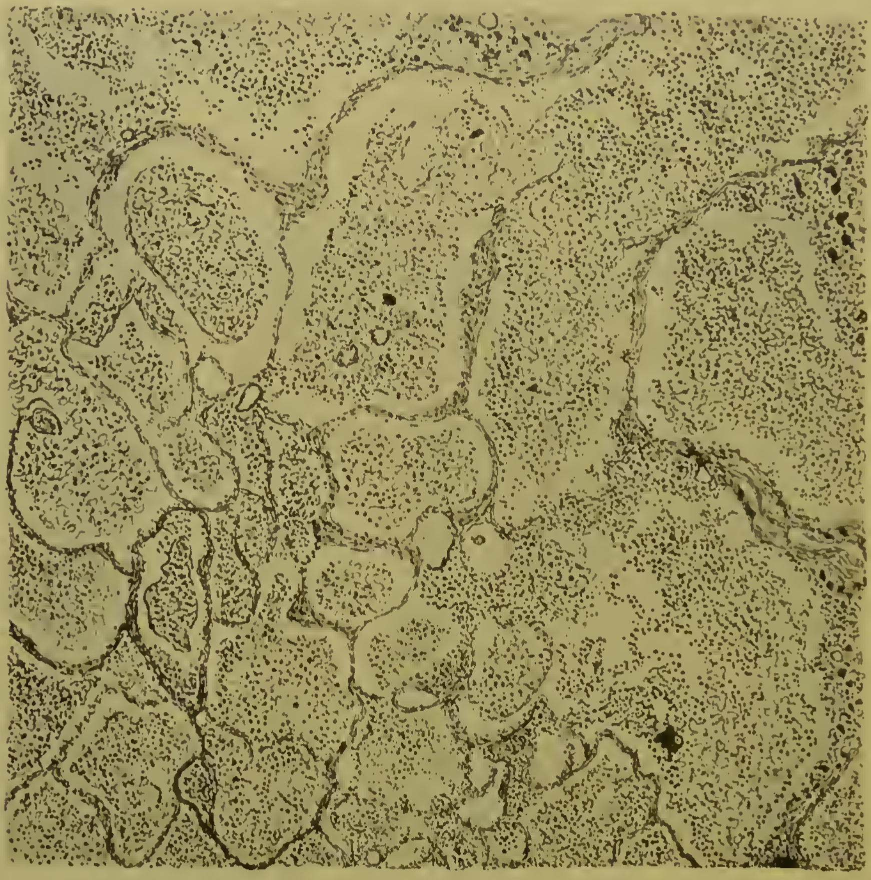


Fig. 116.—Section of Croupous Pneumonia. × 60.

The section shows red passing into grey hepatisation. The alveolar walls are stretched and the cavity of the alveolus is filled with inflammatory material consisting partly of fibrin, partly of migrated leucocytes. Earlier in the disease fibrin is present almost to the exclusion of leucocytes, later the converse is the case. Black irregular particles of inhaled carbon (soot) are scattered through the section.

Corresponding to the red and the grey varieties of hepatisation, we have definite histological pictures; but the stage of congestion, which is very definite clinically, has no definite macroscopic or microscopic characters, probably, because with the cessation of the circulation the congestion disappears.

In **red hepatisation** the pulmonary alveoli are filled with an exudation which has undergone coagulation. The strands of fibrin that are formed interlace in every direction within the alveolus, but are always most closely interlaced close to the alveolar wall, while the meshwork is loosest in the centre. The fibrin is not evenly arranged around the margins of the alveolus, but is thickest at certain points, and these probably correspond to endothelial cells which have died, and therefore have given rise to a 'tissue proteid' which originates the coagulation. In the meshwork of the fibrin are to be found a few leucocytes, one or two endothelial cells, and, perhaps, a small number of red corpuscles, but in typical red hepatisation the number of cells of all kinds in the alveolus is always very small. The alveolar wall has also undergone change. Instead of the wrinkled appearance which is presented by a section of normal lung, the alveolar walls are straightened out, so that the margin of the alveolus is approximately round or oval or quadrilateral with rounded corners. It is this change with which the increase in bulk of the affected lobe has to be correlated. At the same time the alveolar wall is thicker than normal, and shows numerous openings which are the cut ends of capillaries and which may be distended with red blood corpuscles. This change is accountable for the red character of the hepatisation in most cases, but it need not be the sole cause. It sometimes happens that the inflammation is accompanied by a considerable diapedesis of red corpuscles, and these, collecting in the alveoli, play a large share in producing the red colour.

In **grey hepatisation** the appearances are different. The alveoli are filled with solid substances instead of with air, it is true, but the substances are not the same as in red hepatisation. In the first place, the fibrin has entirely disappeared, or, at most, a few small strands are visible here and there. On the other hand, there is present in the alveolus a certain amount of a granular material which is probably disintegrated fibrin. In the second place, the cells which are present in the alveoli along with the granular material are numerous, instead of few, and are almost entirely finely granular oxyphil cells and lymphocytes. A very few endothelial cells are probably present also, being derived from the endothelium which lines the air sacs, but they form quite an insignificant proportion of the whole number of cells in grey as in red hepatisation.

It is common to meet with cases which present a somewhat intermediate appearance between red and grey hepatisation. As the result of the examination of a number of such specimens, we cannot doubt that red passes into grey hepatisation owing to the output of numbers of leucocytes into the air spaces. The exact appearance of the grey hepatisation differs somewhat according as a larger or smaller number of red blood corpuscles enters into the formation of the intra-alveolar material in the stage of red hepatisation. In many instances it is difficult to find a single red corpuscle amongst the leucocytes, but in other cases they are numerous. When this is the case it is easy to see that they are undergoing degeneration. Ultimately they become broken up, and the pigment is carried away by the leucocytes in the form of brown granules. It follows, therefore, that whatever the particular character of the red hepatisation, the changes constituting grey hepatisation are always the same.

(*b*) **Hypostatic pneumonia.**—In hypostatic pneumonia we have a condition which has many analogies with and many differences from ordinary lobar pneumonia. It resembles this condition in that it is liable to affect large tracts of lung substance, but it differs in that its limits are not fixed by the anatomical factors of lobes, but by the mechanical factor of gravity. For the same reason it does not possess the same sharp borders as is usually the case with acute lobar pneumonia, but, commencing in a condition of hypostatic congestion, it shades off into the same, more or less gradually. So, too, instead of affecting the whole of one lobe and leaving the rest of the lung untouched, it affects those portions of the entire lung upon which gravity acts to the greatest extent, and is totally uninfluenced by lobar considerations, other than that it is most commonly met with in the lower lobes on both sides. It approximates in appearance to those forms of lobar pneumonia in which there is a large output of red corpuscles into the alveoli, but it advances further than the majority of these in that the alveoli are found to be crammed with red corpuscles to the practical exclusion of any other kind of cell. It is very doubtful whether it ever passes into a stage of grey hepatisation ; the condition of the patient is such that, when it occurs, it leads to death before time has been given for the appearance of a sufficient number of leucocytes in the alveoli.

(*c*) **Broncho-pneumonia, lobular pneumonia.**—This variety of pulmonary inflammation offers numerous differences from those which have been described above. This fact is indicated by the synonyms ‘ catarrhal pneumonia ’ and ‘ broncho-pneumonia ’ that are given to the condition. In these names of the disease are summed up its principal histological features.

Broncho-pneumonia shows no more regularity of distribution than that which is determined by the fact that it is more commonly seen to affect the two lower and the middle lobes than the upper. This fact depends upon the greater degree to which the upper lobe is expanded in inspiration. Nevertheless the upper lobes are by no means exempt—indeed, one never meets with a well-marked case in which there is not a fair amount of broncho-pneumonia in the upper lobes also. In the same way both lungs are affected, unless it be that the condition is the result of a purely local and, so to speak, accidental condition.

Broncho-pneumonia, as is indicated by its name, is associated with changes in the bronchi. It is even justifiable to say that the entire pulmonary part of the affection is dependent upon an antecedent inflammation of the smallest bronchi. For the condition commences as a bronchitis which involves the tubes in the close neighbourhood of the infundibula and rapidly extends to the air sacs themselves. Since the same terminal bronchus serves a number of infundibula, the ultimate effect of the inflammation is an alteration of a small focus or 'lobule' in the lung. In the case of those lobules which are implicated so far as their bronchi are concerned, but which are, nevertheless, not themselves directly inflamed, the result is the production of collapse. It therefore follows that broncho-pneumonia and collapse are very frequently met in combination. And for the latter reason the patches of broncho-pneumonia and collapse are generally surrounded by zones of compensatory emphysema.

The appearances of a lung which is the seat of broncho-pneumonia are largely those of the collapse and emphysema by which it is accompanied, but in addition there are certain appearances which are somewhat peculiar to itself. Thus a broncho-pneumonic lung is usually pale, owing to the degree of pressure which is exerted upon the blood-vessels by the emphysema and the collection of adventitious material in the foci of inflammation. With these patches of pallor the deep purple and depressed patches of collapse stand out in the greatest contrast. The foci of inflammation themselves may be red in colour or quite pale, but whatever their tint, it is almost always possible to squeeze from their centres a small tenacious mass of material having the appearance of pus. By tracing the bronchi downwards it is found that these tubes are the seat of an extensive formation of mucus which extends to the finest branches, and which, in the later stages of the disease, assumes that yellow appearance with which we are well acquainted.

Under the microscope one of the first points to be noticed is the lack of that generally even appearance which characterises sections of a lobar pneumonia. It is seen that while many of the air sacs are filled, others are but half filled, and yet others are comparatively normal. In the centre of the patch the alveoli are all filled, but the margin of the patch is quite irregular. In the centre, too, can generally be found a section of a bronchiole.

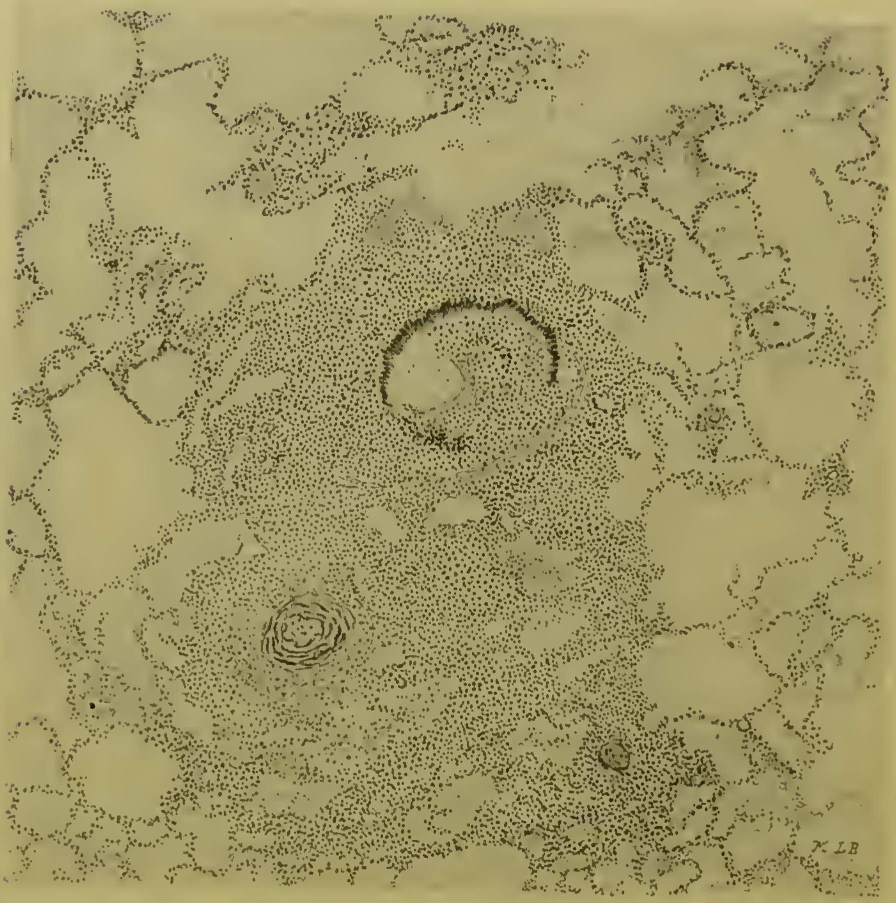


FIG. 117.—SECTION OF BRONCHO-PNEUMONIA. × 80.

In the centre of the figure is a bronchiole of which the desquamated mucous membrane is very distinct; a portion of the fibrous wall of the bronchiole is seen faintly immediately below. The cavities of the bronchiole and of the air spaces with which it is in communication are filled with cells, so that the broncho-pneumonic patch is fairly discrete. In the lower part of the patch is an arteriole. Around the focus of broncho-pneumonia the lung is in a condition of compensatory emphysema.

Around the patch the air sacs are dilated and their walls are thinned owing to the occurrence of compensatory emphysema. The actual size of the patch of broncho-pneumonia varies greatly. In some cases an entire patch comes into the field of the microscope, but more commonly it extends over a large number of fields, and sometimes it is nearly as extensive as a true lobar pneumonia.

So far as the actual composition of the patch is concerned there is much variability, but the main types of broncho-pneumonia are three. The commonest is that in which the alveoli of the lung are filled with a number of cells of the endothelial and the leucocytic types. Of these cells, it is usual for the endothelial cells to be most numerous; they are derived from the lining endothelium of the alveolus, which undergoes proliferation and then desquamates. It is this fact which causes the inflammation to be of the catarrhal type. Although the leucocytes are not so numerous, they are still present in large numbers in most cases. They are principally of the finely granular oxyphil and the lymphocytic variety, and are to be easily distinguished from the endothelial cells by their smaller size, by their more deeply staining nuclei, and by the more irregular characters of the nuclei in the case of the finely granular oxyphil cells. Granules are absent from the cells in most cases. In this variety of broncho-pneumonia marked evidences of the extension of the inflammation from the smaller bronchi are present. For it can always be seen with a little care that the section contains a portion of a bronchiole which is filled with a mixture of granular material, migrated leucocytes in large numbers, and desquamated epithelium. As a rule, the desquamated epithelium is found in a distinct layer; there then lies at some little distance from the

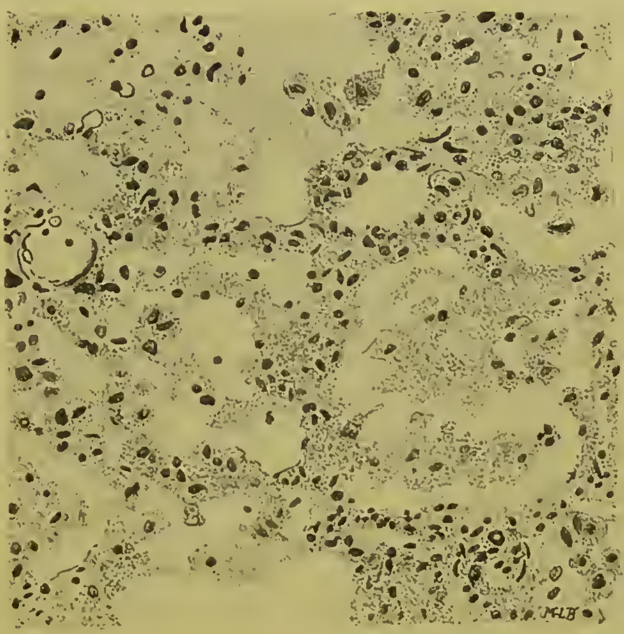


Fig. 118.—Section of Broncho-pneumonia. × 420.

The alveolar wall ar thickened, being infiltrated with exudation fluid and leucocytes (small nuclei); there is proliferation of their endothelial cells (large nuclei). The air spaces are filled with granular material, numerous desquamated endothelial cells, and a very few leucocytes.

wall of the bronchus a more or less well-preserved layer of columnar epithelium, which may also show signs of proliferation previously to its desquamation. In this variety of broncho-pneumonia red corpuscles are present in very small numbers.

The second variety of broncho-pneumonia is almost as common as that which has just been described. It bears a very close resemblance to lobar pneumonia so far as the histological appearances which obtain in the individual alveoli are concerned. That is to say, the air sacs are filled with a fibrinous network in which are entangled varying numbers of red corpuscles and leucocytes. Nevertheless the cells are not present in any considerable numbers, so that the general appearances are more those of red than of grey hepatisation. At times the resemblance is so close that it is impossible to give an opinion as to the actual nature of the inflammation from the examination of a small portion of the section. At a little distance, however, one generally finds a spot at which the appearances are less equivocal.

The third variety of broncho-pneumonia is of a distinctly hæmorrhagic type. In it the alveoli are largely filled with red corpuscles, with which may be mixed a little fibrin and a small number of leucocytes. This variety has great resemblances to the hæmorrhagic form of lobar pneumonia, but as in the case of all forms of broncho-pneumonia, it has a far more patchy arrangement. This variety is less frequently seen than either of the other two.

Broncho-pneumonia, as it has been described in the preceding paragraphs, is particularly a morbid condition of young children, but it may also occur in older persons when some condition has intervened to lower their powers of resistance. Thus it may occur in typhoid fever and in similar prolonged febrile diseases, but it is rarely so extensive as in childhood, and is therefore less frequently fatal. In the case of such diseases, however, as those just mentioned, when death actually occurs it often takes place by way of the broncho-pneumonia.

Inhalation pneumonia.—In patients who are insensible, whether from general coma or from local loss of sensation about the glottis, or who are affected by paralysis of the muscles of the larynx, it is common to meet with a somewhat different variety of broncho-pneumonia which depends upon the inhalation of particles of food, morbid secretion, blood, &c. The number of conditions under which this 'inhalation pneumonia' occurs is very large; it is clear that for its occurrence nothing more is necessary than that foreign bodies should either pass the glottis or should be introduced into the trachea or bronchi below the larynx. Besides the conditions mentioned above, inhalation pneumonia occurs if an aneurysm of the aorta or a malignant growth of the œsophagus ulcerates into the trachea or bronchus. Under any of these circumstances the ultimate result, so far as the lungs are concerned, is much the same.

Inhalation pneumonia differs from the other forms of broncho-pneumonia essentially in the fact that the material which is inhaled is septic, and generally so to an intense degree. In many cases we find that the foci have softened, so that a number of small abscesses with irregular walls are formed, and even if this is not the case to the naked eye, the appearances under the microscope are such that it is clear that a termination in abscess was only anticipated by the death of the patient. For the foci of inflammation consist of little else than aggregations of leucocytes, even the alveolar walls being broken down to a large degree. Where the condition is a little earlier, and especially when the material which has been inhaled is blood, the focus of inflammation shows the presence of a large number of red corpuscles, but there is hardly ever that proliferation and desquamation of the endothelial cells lining the alveoli which is so marked an accompaniment of ordinary broncho-pneumonia. The fact that the condition originates in the terminal bronchi is self-evident from a consideration of the mode of its production, but is also recognisable by the definite implication of the bronchioles as seen under the microscope. The changes are generally found in both lungs, though if the material is introduced into one bronchus the corresponding lung alone may be affected. Even under these circumstances it is, however, commonest for both lungs to be affected, for material coughed up from the one lung is liable to be inspired into the other.

We shall have to consider later a condition which has many resemblances to inhalation pneumonia, but which depends upon lodgment of septic embolisms in the branches of the pulmonary artery. This condition (pyæmic abscess) is, however, generally to be distinguished with ease from inhalation pneumonia, and more particularly by the conditions under which the two forms of disease are liable to occur.

(*d*) **Suppuration.**—(*a*) **Abscess.**—Abscess of the lung is a somewhat rare condition. It is true that the excavation which occurs in pulmonary tuberculosis is nothing more than a special form of abscess formation, but the cavities in tuberculosis are not generally understood when the name 'abscess of the lung' is employed. The condition is most commonly met with in the case of drunkards and other similarly debilitated persons who have recently suffered from lobar pneumonia.

An abscess of the lung is always situated in the midst of a focus of pulmonary inflammation which is indistinguishable macroscopically and microscopically from grey hepatisation. In fact, the simplest case of grey hepatisation is nothing more than a potential abscess, for it consists of innumerable leucocytes aggregated at some spot. The difference lies in the fact that in grey hepatisation the alveolar walls are not injured to such an extent that they undergo disintegration, whereas in abscess they are broken down and fall into the abscess cavity that is thus produced. As a result of the foregoing considerations the abscess cavity is generally found in the centre of a lobe of the lung. It is uncommon for more than one abscess to be present, but then it is generally of considerable size.

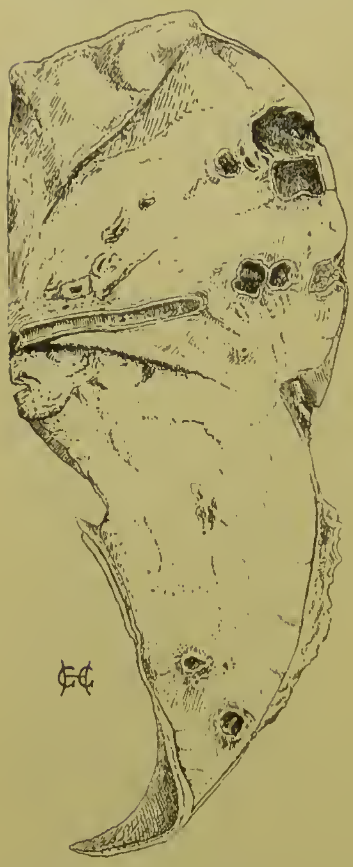


Fig. 119.—Suppurative Broncho-pneumonia. × $\frac{3}{4}$.

Lobe of a child's lung in which the broncho-pneumonic process has gone on to the formation of numerous small abscesses.

(β) Suppurative broncho-pneumonia.—A more common condition, though still not very frequent, is that in which numbers of small abscesses are scattered throughout the two lungs. This condition corresponds to the variety of abscess that has just been mentioned, except that, instead of occurring in the course of an attack of lobar pneumonia, it occurs during the course of broncho-pneumonia. The abscesses are then of small size, and may be situated in the terminal bronchioles or may affect the air sacs with which those terminal bronchioles are in relation. Cases of this kind are chiefly seen in the lungs of young children, and in the subjects of inhalation pneumonia.

When the foci of suppurative broncho-pneumonia are examined carefully, it is seen that all of them are irregular in outline. Some of them are completely solid, and of those which show a central cavity some present an irregular and others a fairly circular cavity. In the case of those in which the outline of the central cavity is irregular we may have to deal with a definite abscess which has formed in a collection of air spaces or one which has commenced within a bronchiole and has extended beyond its walls into the tissue around. But in the case of foci in which the central cavity is bounded by a fairly circular margin, we almost always have to deal with a bronchiole the walls of which are still to some extent intact. The bronchiole is locally dilated, and its walls are markedly infiltrated with inflammatory products, while the lumen is filled with a material which is but little removed from ordinary pus. The condition, that is to say, is one of bronchiectasis of acute suppurative origin. It arises partly because the walls of the bronchiole are weakened by the inflammation going on within the lumen, and partly because the support which is normally given to the bronchiole by the surrounding pulmonary tissue is removed owing to the changes which are there going on. As a consequence of these two factors the intra-bronchial pressure which is got up during cough, for example, produces a greater dilatation of the weakened spot than normal, and the elasticity of the wall being impaired, the recoil is also diminished. In suppurative broncho-pneumonia the formation of these small acute bronchiectases is common.

(γ) **Pyæmic abscess.**—The lungs may also be the seat of abscesses arising during the course of pyæmia. In this case the focus around which the abscess forms is an embolus derived from some part of the venous system and containing pyogenetic micro-organisms. The commonest situation for the primary focus of disease is the uterus, but any other region of which the veins are systemic may serve. In the case of primary disease of the abdominal area leading to pyæmia, the abscesses are generally formed in the liver, but even then it is possible for a tertiary infection of the lungs to occur. As a rule, pyæmic abscesses of the lungs are of considerable size; they are always surrounded by a zone of tissue which is consolidated in the same way as in the formation of other varieties of abscess. Pyæmic abscesses of the lungs are usually found in the lower lobes, and generally close to the bases. The condition usually commences as an intensely acute septic pneumonia with so great an extravasation of red blood corpuscles as to belong to the hæmorrhagic type. In fortunate cases, resolution of such a pneumonia may take place without the formation of an abscess.

(ε) **Gangrene.**—Gangrene of the lungs is not a very common condition, and even when it occurs it is rarely more than a portion of one lobe that undergoes gangrene. Most commonly the focus of local death is in the lower lobe, and at some little distance from the pleural surface, although the inflammation which surrounds the dead tissue extends to, and involves, the pleura itself. Occasionally it is found that the entire lung has undergone gangrene, but this is excessively rare.

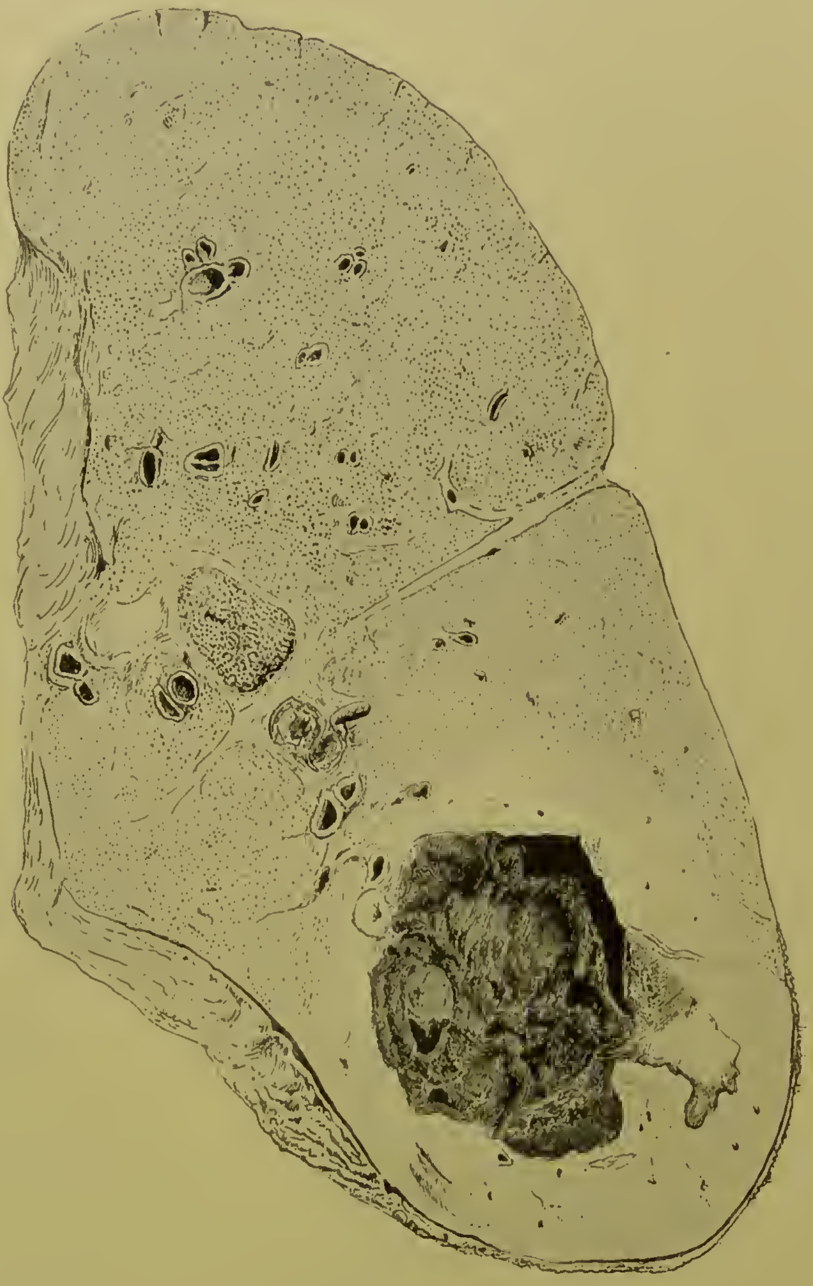


Fig. 120.—Gangrene of Lung. × $\frac{2}{3}$.

In the lower lobe is a black gangrenous mass which is partially separated along its upper border. The lung tissue surrounding the mass is in a condition of grey hepatisation.

The gangrenous portion of tissue is of a black colour and of a wash-leather consistency in the earlier stages, but pultaceous later. Its odour is most offensive. As a rule, it is still joined to the surrounding tissue, although it may be clear that a commencement of separation has taken place with the formation of a cavity having irregular and sloughy walls. It is very uncommon to find any evidences of repair, but on the other hand it is general for a large portion of the surrounding lung to be consolidated, and evidently in a condition closely bordering upon abscess or gangrene itself. Gangrene, like abscess, is particularly apt to occur in persons of poor constitution or low state of health, especially if they have become attacked by lobar pneumonia.

The microscopical appearances of gangrene of the lung are similar to those of gangrene elsewhere. That is to say, there is little evidence to inform us as to the nature of the tissue involved, and such cells as are present are degenerated, their protoplasm granular and their nuclei broken up, indistinct, and badly staining. The same features are present in the tissue which borders on the gangrenous patch, but which is not itself actually gangrenous.

Further out there begins to be a little more differentiation of the tissue. The cells, although greatly affected, are not entirely disorganised, and it begins to be possible to distinguish between the lung tissue proper and the material which fills the air spaces. Still further outwards the changes are those of an ordinary grey hepatisation. It is not very common to find that the appearances more peripherally show a tendency to belong to the red hepatisation variety, but this may perhaps be seen in an adjacent lobe of the lung.

(*f*) **Fibrosis.**—When a portion of lung tissue has become injured and has suffered inflammation, as in the case of other tissues, there may be a formation of reparative fibrous tissue. It does not, of course, matter what the form of irritation and inflammation may have been, so long as it was of an intensity insufficient to lead to either a complete destruction of the lung or a continuance of the inflammation in an acute stage until the death of the patient. But, nevertheless, the occurrence of fibrosis is practically confined to cases of tuberculosis, syphilis, cases in which the lungs have been subjected to a chronic inflammation owing to the inhalation of fine particles of dust (the **pneumokonioses**), and a few cases of lobar pneumonia. In all these cases the change consists in the new formation of cicatricial fibrous tissue, but the macroscopic pictures produced vary considerably in the different cases.

The situation at which the new formation of fibrous tissue takes place is naturally determined by the situation at which the irritant has been acting. Hence we find that in the pneumokonioses fibrosis is far more general than it is in tuberculosis where the inflammation is largely local. The same is true in those cases of lobar pneumonia which terminate in fibrosis. Here, the fibrosis is practically limited to the lobe which was affected.

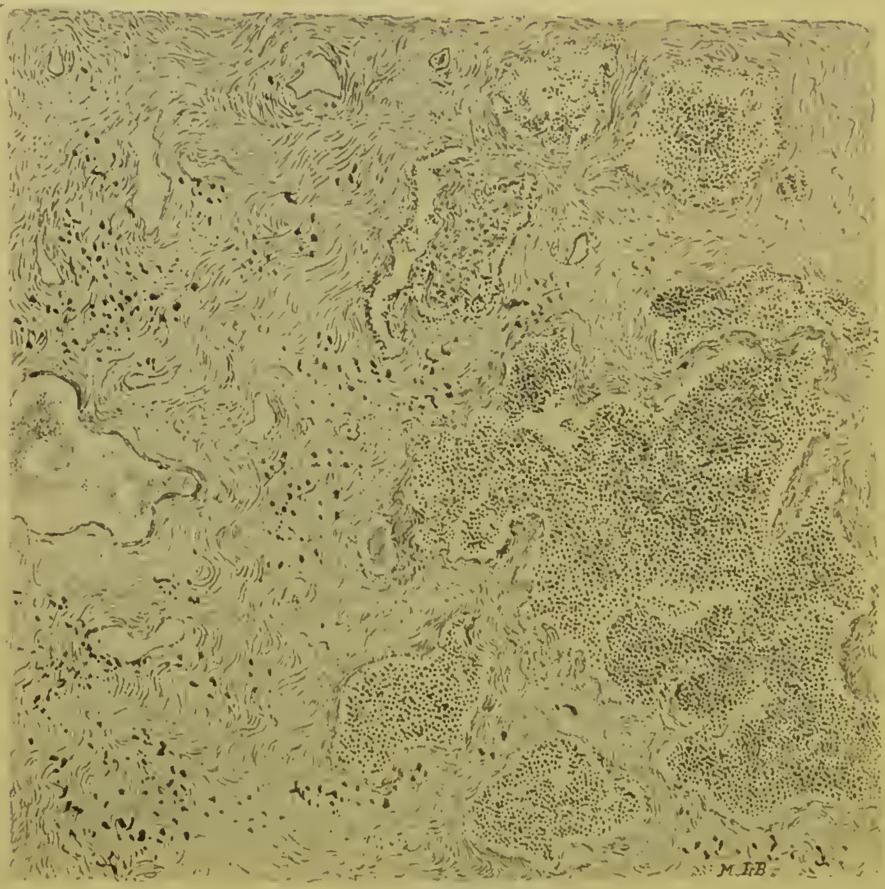


FIG. 121.—SECTION OF FIBROID LUNG. × 60.

The condition is one of fibroid tuberculosis with broncho-pneumonia, but definite evidences of the tuberculous process are not seen in the section. The great increase of fibrous tissue carrying blood-vessels and black carbonaceous particles is well seen. The condition of acute inflammation with this magnification might be either that of grey hepatisation or of broncho-pneumonia, as it is impossible to see whether the nuclei present in large numbers are those of leucocytes or of endothelial cells.

The fibrous tissue is generally most extensively developed in the situations of the ordinary fibrous-tissue septa of the lung. Hence it has a tendency to be thickest at the root of the lung. This is particularly the case with the fibrosis that occurs in syphilitic disease of the lung. In tuberculosis there is generally a most considerable formation in the centre of the upper lobes, and then the contraction of the fibrous tissue leads to a puckering of the surface of the lobe which is highly characteristic of arrested or receding tuberculosis. In the pneumokonioses not only is the arrangement of the fibrous tissue more general, but also, as a rule, the strands of the meshwork produced are finer and the meshwork itself is finer also. Nevertheless it is common to find that broad bands of dense fibrous tissue pass from the root of the lung into the substance of the different lobes, keeping more or less closely to the positions of the normal septa.

Microscopically, a fibrotic lung generally shows that the fibrosis is only a part of the actual changes that are present. Although it may appear to the naked eye that there is an absence of any acute inflammation, the microscope almost always reveals the existence of a considerable amount. This acute inflammation may be of the pneumonic or of the broncho-pneumonic type, and in the case of fibrosis associated with tuberculosis it is very likely to be of the tuberculous type. As a rule, we find that the alveoli in the neighbourhood of the masses of fibrous tissue are filled with a mixture of leucocytes and endothelial cells, so that the appearances are very similar to those of certain forms of broncho-pneumonia or to grey hepatisation. In addition, the traction of the fibrous tissue, and the fact that a portion of the pulmonary tissue has been destroyed, have led to a certain amount of compensatory emphysema around the fibrous mass, so that the alveoli are not only filled with products of inflammation, but are also larger than normal and have thinner walls. Evidence that the fibrous tissue has replaced lung tissue is given by the fact that the fibrous tissue, however dense, contains a certain amount of the sooty material which is constantly found in the lungs of those who have lived in cities and in large towns. To the presence of particles other than soot we shall have to refer immediately.

Although the occurrence of calcareous deposits in masses of fibrous tissue is, so to speak, an accident, it occurs frequently under certain conditions. It may almost be taken as certain that a mass of dense fibrous tissue in the lungs in which calcium salts are deposited is evidence of a former tuberculous inflammation. However considerable the amount of fibrous tissue may be, it is very rare for calcareous deposits to occur in connection with any other disease.

The pneumokonioses.—The members of the group of pneumokonioses produce different pictures according to the nature of the dust which has been inhaled. Where it consists of particles of carbon, as in the case of miners, the lung is completely black.

The particles, too, are of larger size than those which are found in the lungs of dwellers in cities. Moreover in the latter instance the pigmentation is never the actual cause of a fibrosis, although it is often an accompaniment. In the case of stonemasons the fibrosis is accompanied by a pinkish-grey colour of the lung, while amongst those who are exposed to the chance of inhaling large quantities of particles of iron, the lungs are not only fibrotic, but also of a rusty red colour. In all cases, however, the general distribution of the fibrosis is the same. One distinction must be made in the case of those persons who are the subjects not only of pneumokoniosis but also of tuberculosis. Many of the persons who are exposed to the inhalation of large quantities of dust are also the subjects of pulmonary tuberculosis. Perhaps, indeed, the fibrotic condition of the lung predisposes it to the reception and harbouring of the tuberculosis bacillus. In any case it is not uncommon to find that, in addition to a general fibrosis that must be ascribed to the action of the dust, there is a fibrosis that must be ascribed to a chronic tuberculosis. Possibly because the individuals who are attacked are older, tuberculosis in those who are the subjects of one of the pneumokonioses is particularly apt to be of a fibrotic type.

(7) **Specific inflammations**—(*a*) **Tuberculosis.**—When an attempt is made to tabulate the different manners in which tuberculosis may affect the lungs, and the different appearances that it may produce, a sufficiently imposing list can be drawn up. But if it be considered that the process is nothing more, fundamentally, than a variety of inflammation, it is clear that the formation of such a list rather impedes than furthers a proper understanding of the condition. For this reason we shall mention as few varieties of pulmonary tuberculosis as possible.

The fundamental basis of tuberculosis being the 'tubercle,' it is in the different arrangements of the tubercles and the subsequent changes that they undergo that the different varieties of tuberculosis consist. Thus we may meet with isolated tubercles of small size, or we may find them aggregated into masses; we may find that these masses have undergone degenerative changes in the centres, or that their progress has been arrested, and that they have become surrounded by cicatricial tissue, and, lastly, we may find that this cicatricial tissue has, in its turn, become altered. But with these changes the possible variations of tuberculosis are practically concluded.

The conditions which have been mentioned above account for the principal characters of the disease as we meet it in the post-mortem room. It will therefore serve for our present purpose if we confine our attention to (*a*) miliary tuberculosis, (β) caseous tuberculosis, (γ) tuberculosis with excavation, and (δ) fibroid tuberculosis.

(*a*) **Miliary tuberculosis** is a condition in which the lungs are studded with tubercles the size of a millet seed. The condition is always more or less general throughout the lungs, and, in a large number of cases, general throughout the entire system. The tubercles themselves are of about the same age everywhere, and may either appear as small grey semi-translucent masses having a shotty feel, or they may be somewhat larger and be of a distinctly opaque yellow colour. The actual number that is present in the lung varies enormously. In one case they may be scanty, but in the next they may be packed together very closely. Whenever they are present in more than very small numbers the intervening lung tissue is congested, and even when they are few in number it is possible to distinguish that each tubercle is surrounded by a fine ring of pulmonary tissue which is redder than the rest.

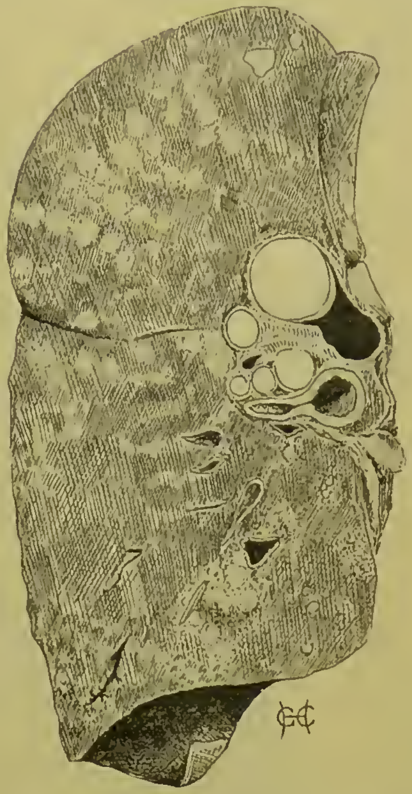


Fig. 122.—Caseous Miliary Tuberculosis of Lung. $\times \frac{3}{4}$.

From a child who died of generalised miliary tuberculosis. Numerous caseous foci the size of hemp seeds and less are studded through the lung, particularly the upper lobe. At the root of the lung are five caseous lymphatic glands, the largest of which is encroaching upon the pulmonary vein. It is usually owing to the rupture of such a gland into a vein that the disease becomes generalised.

(β) **Caseous tuberculosis** is, strictly speaking, not confined to that variety which is called by the name. For it is very common to find in the case of miliary tubercles that some or even the majority have become caseous in the centre. But in the variety which is definitely termed caseous, the affected portion of lung is much larger and is of a uniform yellowish-white colour. Its consistency is altered, for the position of the former spongy lung tissue is now occupied by a consolidated mass of cheesy material.

Caseous tuberculosis may present itself in a variety of ways, but the two commonest are that in which numbers of aggregated tubercles are scattered throughout the lung, and that in which a large mass of lung is consolidated and of a yellow colour, so that the arrangement recalls that of lobar pneumonia.

The lobar arrangement we may meet with in any part of the lung, although it most commonly affects the upper lobe. It is found, however, not infrequently at the base of the lower lobe, and sometimes the entire lung is affected throughout. The discrete variety shows a much greater tendency to affect the upper part of any lobe, but most particularly the upper part of the superior lobes. It is general, indeed, to find that the lung presents a series of gradations between a condition of excavation such as will be described in the next paragraph and a more or less discrete caseous miliary tuberculosis. That is to say, there is a cavity at the apex of the upper lobe, and perhaps at the apex of the middle or lower lobe, while the material surrounding the cavities consists of an undifferentiated caseous mass, and at a distance are numbers of small foci of caseous tubercle, the individual outlines of which are not, as yet, entirely merged in

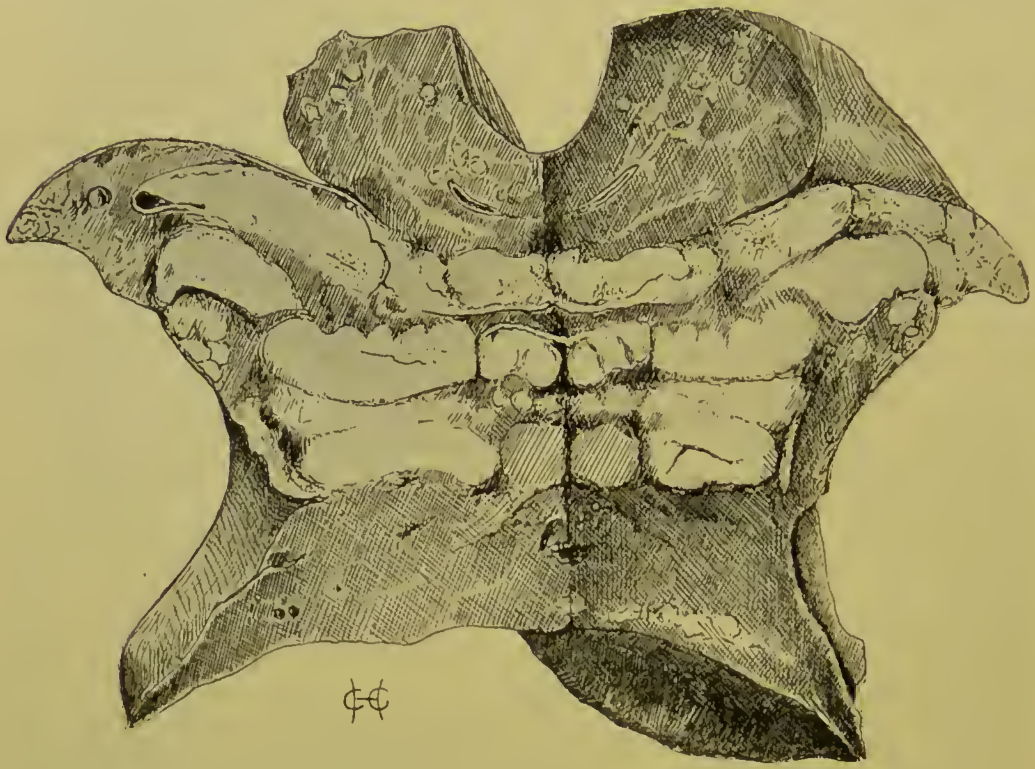


Fig. 123.—Extreme Caseous Tuberculosis of Lung. Natural Size.

A mass of caseous material extends from the lymphatic glands at the root of the lung into the substance of the organ, and replaces the greater part of the lower lobe. The direction taken by the mass corresponds with that of the main bronchi. There is a small amount of caseous tubercle in the remainder of the lung.

the general mass. An appearance of this kind forms one of the commonest pictures of a fairly acute pulmonary tuberculosis. Caseous tuberculosis of the lobar type (caseous pneumonia, as it used to be called before its definitely tuberculous nature was fully recognised) is a far less common variety. Like the discrete variety, it is liable to go on to extensive excavation.

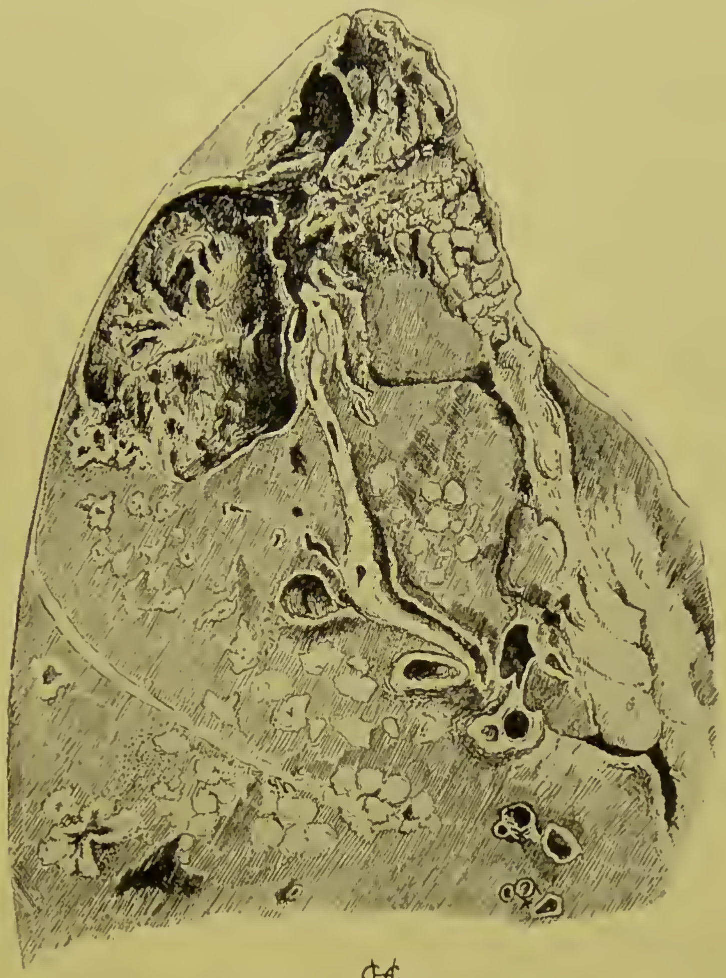


Fig. 124.—Tuberculosis of Lung with Excavation. $\times \frac{3}{4}$.

The apex of the lung is occupied by an irregular cavity which reaches up to the pleural surface. Below are seen caseous foci, some of which have broken down into small cavities in the centre. The bronchial walls are greatly thickened. The upper and lower lobes of the lung are adherent by a well-marked band of dense fibrous tissue.

(γ) **Tuberculosis with excavation** is the usual form in which we meet with the disease in the lung. When a mass of tubercles has undergone caseation, it may remain unaltered except for a certain amount of drying up and an encapsulation by inflammatory fibrous tissue, and, perhaps, an infiltration with a larger or smaller amount of calcareous material. But this is not the rule. The rule is for the caseous material to become still further softened, and, finding its way into a bronchus during its process of extension, to be gradually removed by expectoration. This process of excavation is aided to a large extent by the subsequent changes which occur in the walls of the cavities (**vomicæ**) thus formed. For it is clear that the interior of the cavity is in direct communication with the outer air, and, therefore, that there is a great liability for putrefactive and other micro-organisms to gain access to it, and lead to further breaking down of the dead and dying tissue of which the wall of the cavity is composed. How far the occurrence of this contamination aids in the excavative process we do not know, but it is probable that it plays a very important part.

The cavities that occur in pulmonary tuberculosis are of different kinds according as they are recent or chronic, and according as they have been formed rapidly or slowly. So far as size is concerned, they vary indefinitely. We may meet with them so small that they are almost microscopic, or so large that the entire lung is converted into one huge cavity. In an ordinary case we shall find that the greater part of the upper lobe on one or both sides is almost completely excavated by the formation of a number of vomicæ that have broken into one another.

The chief difference between a cavity that has been formed rapidly and one which has been formed slowly lies in the characters of their walls. When the cavity has been formed rapidly the softening has generally taken place in a mass of caseous tubercle of the pneumonic type. Hence a large amount of tissue is available for breaking down, and the wall of the vomica is irregular and ragged, and consists of thick caseous material. On the other hand, when the cavity has been formed slowly, the tissue by which it is surrounded is of a far more fibrotic type and the wall of the cavity tends to be smooth. At the same time there is a liability for the process of excavation to spare somewhat the more resistent elements, so that the blood-vessels in particular are apt to be found lying in the wall of the vomica or perhaps traversing it from side to side. This latter fact is one of the greatest importance, for the walls of the vessels, although preserved, are weakened both by the changes that they have undergone and by the removal of that pulmonary tissue which normally supports them. They are therefore liable to become locally dilated into aneurysms, and, ultimately, to rupture. This rupture is accompanied by the outpouring of a large quantity of blood, and accounts for the most common variety of hæmoptysis. When hæmoptysis occurs in the absence of definite excavation, it is probable that it is capillary and depends upon the engorgement which accompanies the laying down of the tubercles. It can easily be understood that the hæmoptysis that occurs along with excavation arises from the opening of an artery. So far as is known the veins do not enter into the production of hæmoptysis; their walls are so thin that thrombosis has occurred within them long before the ulceration has extended through the walls themselves.

(δ) **Fibroid tuberculosis.**—This variety of tuberculosis is of two types that are fundamentally different, although the pictures presented by the lungs are very similar in most cases. The fundamental difference lies in the fact that in the one variety the fibrosis is definitely cicatricial and is comparable to the scar which is formed after a certain loss of material has taken place in any tissue, while in the other variety the fibrosis is antecedent to the tuberculosis altogether, and is dependent either upon some one of the pneumokonioses or upon syphilis.

So far as the actual appearances are concerned, the chief difference lies in the fact that when the fibrous tissue is cicatricial it is liable to be more localised about the seat of tuberculosis, whereas in cases of primary fibrosis the fibrous tissue is distributed throughout the lung with a greater degree of evenness. So far as the tuberculous disease itself is concerned, it is common to find that when the fibrous tissue is cicatricial the process has extended to the stage of excavation, although the cavities themselves may be small. In the other variety of fibroid tuberculosis the tuberculosis may be in any stage.

A certain amount of cicatricial fibrosis is very frequently found in cases of tuberculosis that have proceeded to the stage of excavation, but it must not be supposed that this is always the case. On the contrary, it is only in cases that are of long standing that the formation of fibrous tissue reaches to any considerable point. These are the cases in which the cavities are apt to be of the smooth-walled type, and small.

Pulmonary tuberculosis of all kinds is very liable to be associated with pleurisy and the formation of pleuritic adhesions. It is necessary to mention this point here, but the actual description of the pleural changes will be postponed until we come to consider the pathological anatomy of these spaces.

(*b*) **Syphilis.**—The lungs are not very often found to be the seat of syphilitic manifestations, but when they are, the disease may appear either in the form of a general fibrosis which is densest at the roots, or in the form of gummata. Of these two modes a general fibrosis is the more common, but to it no particular attention need be given here. Neither is it necessary to delay over the consideration of gumma. For a gumma of the lung merely consists of a mass of caseous material similar to that which is found in the gumma of the liver. The important point lies in the differentiation of gumma from a focus of caseous tuberculosis. The lack of any particular tendency to affect the apex of the lung, the much smaller tendency to undergo softening, and the comparatively sharp limitation of a gumma, are generally sufficient to effect a diagnosis. The diagnosis between gumma and certain other allied conditions (e.g. glanders) is, however, frequently very difficult, or even impossible without assistance derived from the history of the case, &c.

(*c*) **Actinomycosis.** — Although the lung is not very frequently attacked by actinomycosis, the changes which are produced when this does occur are formidable. The fungus produces a form of granulation tissue which readily undergoes caseation of a particularly soft type, or, more generally, undergoes a conversion into definite abscess cavities. Thus the lung becomes riddled from apex to base with ragged and irregular cavities, the pus of which frequently contains the small characteristic grains of the fungus. The condition is generally mistaken for tuberculosis or new-growth until the discovery of the characteristic grains in the purulent expectoration sets the diagnosis at rest. The inflammatory process is liable to extend through the pleura and thoracic wall and appear on the surface of the chest.

(*d*) **'Pseudo-tuberculosis.'** — Inflammatory conditions of the lungs are known which do not come into any of the classes that have been described, but which bear so many resemblances to tuberculosis that they have been collectively referred to under the name of pseudo-tuberculosis. The name is a bad one, for a morbid condition is either tuberculous or it is not. In a large number of cases a prolonged examination reveals the presence of the bacillus of tuberculosis, but in the remainder this micro-organism is not found. On the contrary, micro-organisms differing from the bacillus of tuberculosis are present. Sometimes these are bacilli that have resemblances to the tubercle bacillus, but often they are totally different, being, perhaps, streptothrices; in the lower animals, small worms may be found.

The changes to which these agents give rise consist in a broncho-pneumonia, which is liable to undergo central softening, caseation, or other degenerative alteration. Since tuberculosis is fundamentally nothing more than a special variety of broncho-pneumonia which undergoes a somewhat special form of degeneration, it is clear that the macroscopic pictures of pulmonary tuberculosis and the so-called pseudo-tuberculosis may be, at times, practically identical. There is no doubt that the name 'pseudo-tuberculosis' will ultimately die out, and that the various conditions which are to-day grouped together under the name will be referred to their proper classes. At the present time the matter is rendered even more difficult by the fact that certain bacilli that are met with more frequently than others in connection with cases of this description, have been definitely named **B. pseudo-tuberculosis** by some French authors.

(8) **New-growths.**—Primary new-growths of the lungs are excessively uncommon. The least rare are carcinomata, which arise in connection with the epithelium of the bronchial tubes and form white soft masses, and lead to the appearance of metastases both in the rest of the lung and in the bronchial glands.

Secondary new-growths are common, and may be either carcinomata or sarcomata. In a large number of cases these secondary growths arise in connection with the blood-vessels, the generalisation of the growth taking place by way of the blood stream. The secondary nodules are usually round and have the characters of the primary growth. Hence we find that a secondary growth of an osteo-sarcoma in the lung contains bone; of a chondro-sarcoma, contains cartilage; while a hæmorrhagic sarcoma of the testis, for example, also forms highly hæmorrhagic metastases in the lungs. Direct extension of a pleural endothelioma or a mediastinal lympho-sarcoma into the lung is the rule.

The growth of a metastasis leads to the destruction of the portion of the lung which it replaces, but at the advancing edge it is seen that the process commences by the penetration of the cells of the growth into the alveoli of a lung without a destruction of the alveolar walls themselves. But, in addition to this definite malignant infiltration, the growth acts as an irritant to the tissues around, and we always find that there is present a certain amount of a typical and indifferent broncho-pneumonia in advance of the growth. (Fig. 42.)

Animal parasites are but rarely found in the lungs. Of them hydatids are the most important, and sometimes they give rise to the formation of cysts of considerable size. The foregoing statement is true only for man. In some of the lower animals, such as the pig and sheep, it is very common to find that a broncho-pneumonia is present which has been caused by worms. In these cases the worms are found in the small as well as in the large bronchi.

(4) THE PLEURÆ AND PLEURAL CAVITIES

Although it may fairly be said that the pleuræ and pleural cavities are more frequently the seat of pathological change than any other tissue of the body, at all events in temperate climates, the number of actual changes to which they are liable is small. Practically we find that the changes incident to or subsequent to inflammation constitute the bulk of the diseases, while the collection of fluid in the cavities, which may or may not be associated with inflammation, and the occurrence of new-growths come a long way behind. And yet these processes constitute the entire list of the morbid processes affecting the pleuræ with which we shall have to deal here.

(1) **Inflammation** of the pleura (**pleurisy** or **pleuritis**) may arise directly in the pleura as its primary seat, or it may arise in connection with some disease commencing in another part.

Of these two varieties, secondary pleurisy is far the more common. Indeed, it is decidedly rare to open the thoracic cavity of an adult without finding pleuritic adhesions present in larger or smaller quantity.

The commonest seat for the primary disease upon which the pleurisy becomes engrafted is naturally the lung. But in certain diseases—for example, the different varieties of inflammation of the kidney—it is not uncommon to find that the pleuræ become acutely inflamed without the participation of the lung, except so far as that portion is concerned which lies immediately beneath the affected pleura and is obviously affected later.

(*a*) **Acute pleurisy** is characterised by a replacement of the normal shining appearance of the serous surface by a roughened appearance. This is due partly to the presence of a number of tags of fibrin derived from the inflammatory exudation, and partly to changes which occur in the membrane itself. In addition there is generally present a certain amount of fluid in the pleural cavity. This fluid may be present in so small a quantity that the pleurisy is spoken of as ‘dry’—on the other hand, it may be present in sufficient quantity to constitute a pleural ‘effusion.’ It may be perfectly clear, and then it is generally of a pale straw colour, or it may contain flakes of fibrin that are sometimes of considerable size. Red blood corpuscles are rarely present in any considerable numbers.

Histologically, two varieties of pleurisy are to be recognised, according as the endothelial cells normally covering the pleural surface are situated beneath or on top of the fibrinous exudation.

In those cases in which the fibrinous deposit is clearly lying upon the endothelial surface, it is often possible to peel the deposit off with ease and leave a fairly smooth surface beneath. If a section be made of such a pleurisy at right angles to the free surface of the lung, it is seen that the 'false membrane' consists of strands of fibrin in the meshwork of which lie a certain number, usually small, of white and red corpuscles. So far as the tissue of the pleura itself and the underlying lung are concerned, it is not possible to see in such a section much more than that they are swollen and somewhat congested. But if we cut the sections *parallel* to the free surfaces of the pleura, it becomes clear that the membrane is intersected in all directions by capillary blood-vessels which are widely dilated and distended with blood. This vascular layer is, however, of no great thickness. Beneath it there is a small amount of fibrin which lies chiefly in the small and thick-walled pulmonary alveoli that form the under surface of the visceral pleura. In those cases in which the endothelial cells lie superficially to the 'false membrane,' the latter is much thicker and cannot be readily detached. Moreover, it does not entirely consist of fibrin, as in the other case, but the fibrous tissue of the pleura itself enters largely into its composition. This fibrous tissue, however, is not normal, for its constituent fibrils have swollen up and become hyaline. In addition, they cease to take up the ordinary stains for fibrous tissue, but take up readily the characteristic stain for fibrin. For this reason they have been said to undergo a 'fibrinoid' change. There is generally a considerable amount of congestion.

It must not be supposed that the endothelial covering of the pleura is normal in either of the above conditions. On the contrary, it is only present here and there, even in cases in which the pleural tissue is least altered; over large areas it has completely disappeared owing to desquamation.

Whatever the particular characters of the pleurisy, the compressed lung tissue which constitutes the deeper layer of the pleura shares in the inflammation. The changes which it undergoes consist in the filling of the small alveoli with exudation and cells, and the consequent production of an appearance which generally recalls that of lobar pneumonia in the stage of red hepatisation. These changes are far more obvious in sections made parallel to the free surface of the lung than in those made at right angles.

Acute pleurisy of the kinds that have been described above may affect the entire pleura or may be localised to a small portion of the membrane.

(*b*) **Empyema.**—Under certain circumstances, and particularly in cases of acute pleurisy amongst young children, the inflammation goes on to the formation of pus (**empyema**). Apart from the fact that the pleural cavity contains pus, the differences between the actual changes in the layers of the membrane itself are not greatly different from what they are in a non-purulent pleurisy. There are present, however, far larger numbers of leucocytes in the pleura, and in addition (if the case is not too chronic) numbers of diplococci (pneumococci) will probably be found in the pus and can be obtained from it in practically pure culture. As a result of the presence of a larger number of leucocytes in the pleural layers, the membrane has a yellow opaque appearance, and the deposit on it is often of considerable thickness. An empyema may be general or it may be localised. Frequently the suppurative process extends to the pericardium.

Pyopneumothorax.—In addition to the pneumococcus as a cause of suppuration in the pleural cavity, we also find that pus is produced when a tuberculous vomica opens into the pleural cavity. In this case we have the pleural cavity containing air as well as pus, so that the condition is known as *pyopneumothorax.* The micro-organisms present in a pyopneumothorax are chiefly the ordinary bacteria of suppuration and putrefaction.

A pyopneumothorax is of necessity a somewhat chronic condition owing to the difficulty of evacuating the abscess cavity. In addition to being formed as the result of the rupture of a tuberculous cavity into the pleural space, it may arise from the rupture of an empyema into the lung and its evacuation through a bronchus.

(*c*) **Chronic inflammation** of the pleura covers a considerable number of conditions, and merges into that in which there is a formation of fibrous adhesions passing between the two layers of the membrane.

A pleuritic inflammation of some kind, whether more acute or more chronic, occurs whenever the lung itself is the seat of a morbid change. This is particularly the case when the morbid change is associated with the presence of irregularities which can act upon the pleura in a more or less mechanical way. Hence we always find that pleurisy is present in cases of pulmonary tuberculosis and in malignant disease of the lung. For in these diseases nodules are formed immediately beneath the pleura which irritate the membrane and lead to an infection, in most cases, of the opposite layer at the point of friction. In a tuberculous or a malignant pleurisy, therefore, we always find that the special nodules are actually present in the layers composing the altered and thickened pleura.

In cases of the above description the process is generally a slow one and consequently is associated with a considerable new formation of inflammatory fibrous tissue. Moreover, since the changes occur in both layers of the pleura, and since a part of the changes consists in a destruction of the endothelial cells which normally cover the membrane, it follows that such fibrous tissue as is formed tends to bind the two layers of the pleura together. In other words, two granulating surfaces are apposed. To a greater or a less extent, therefore, the cavity of the pleural sac becomes obliterated and the layers of pleura become adherent. At first the adhesions are broken down with fair ease, but as time goes on they become very dense. Frequently also calcium salts are deposited in them, and we may have a thick calcareous plate binding the lung to the thoracic wall.

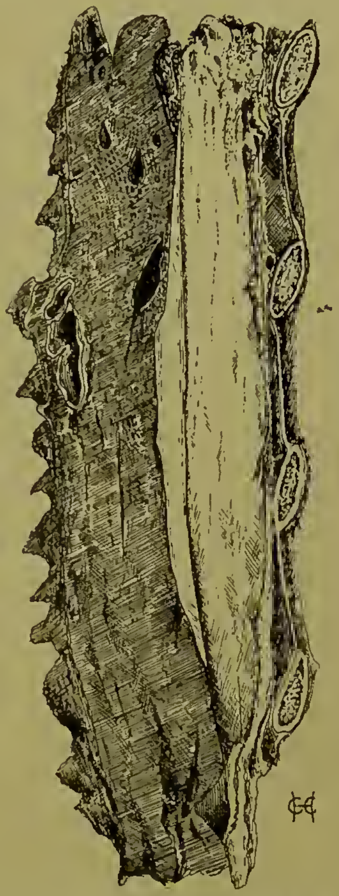


Fig. 125.—Calcification of Pleuritic Adhesions. × $\frac{3}{4}$.

On the right of the figure are seen the sections of four ribs, on the left a portion of the lung, and between these is a white mass of calcareous material.

(2) **New-growths.**—By far the larger number of new-growths of the pleura are secondary and reach it by extension from the lung. For the same reason they are almost always malignant. It may be mentioned here that such nodules of malignant growth in the pleuræ are liable to give rise to the outpouring of a considerable amount of fluid. This fluid contains a large number of red corpuscles, and the fact is highly characteristic, although not pathognomonic, of malignant disease.

The pleuræ are subject to a primary form of malignant disease, viz. endothelioma. When it occurs the pleura is enormously thickened and generally of cartilaginous hardness. In some cases, however, the growth is cellular and the pleural mass is of softer consistency.

Macroscopically, it is often impossible to say more than that the pleural cavity is obliterated by a material which resembles ordinary firm fibrous-tissue adhesions. On close examination it appears that the mass, unlike adhesions, extends into the true pulmonary substance. Definite invasion of the lung, with the formation of nodular masses or of strands of new-growth, is somewhat rare. The most that happens is usually a superficial invasion. The bronchial glands are liable to be considerably enlarged from infiltration with the growth. The microscopic appearances are those of an endothelioma; generally the pleural growth itself is fibrotic and cells are scanty.

SECTION XIII

THE THYROID BODY

The thyroid body is but little liable to disease, and of all the pathological changes which it undergoes inflammation is one of the rarest.

(1) **Atrophy.**—Two conditions are known under which the thyroid body undergoes atrophy. The first is congenital and occurs in the cretinoid offspring of goitrous persons. In cretins we have a profound alteration of the physical and the mental functions of the patients. The individuals are stunted, their heads are usually abnormally large, their intelligence is of a very low order, and frequently they are idiots. The thyroid body is generally very small or practically wanting, but sometimes a mass of tissue is present which occupies the normal situation of the thyroid body and may during life be mistaken for it. When such a mass of tissue is examined microscopically, it is found to consist of little else than fibrous tissue, with, perhaps, a few small representatives of normal thyroid acini, and some colloid material.

In the second variety the change in the thyroid comes on in adult life. As a rule, the fact that the thyroid has undergone change is not recognised until physical and mental alterations have taken place in the patient which have directed attention to the point. These changes constitute the disease known as **myxœdema**, and are very similar to those of cretinism, only far less marked. At the same time they have certain special characters which serve to distinguish the disease from other conditions with which it has superficial resemblances. In myxœdematous atrophy of the gland the diminution in size is always considerable, so that it is possible to determine the fact by examining the throat of the patient. Microscopically the change consists largely in a fibrosis, the true glandular structure having disappeared, and only a small number of shrunken acini, with a little colloid material in them, remaining to indicate the former structure.

(2) **Enlargements.**—Some of the enlargements of the thyroid are of the nature of hypertrophy, but the larger number come far more into the class of pseudo-hypertrophies and are essentially atrophic in their nature.

Of the enlargements which are closely allied to the hypertrophies, the most important is that which occurs in the disease known as **exophthalmic goitre** from two of its most marked features. In this disease the gland is large, soft, and it frequently pulsates during life. The increase in size affects the whole gland, as a rule, including the isthmus, and is dependent upon a hyperplasia. At all events, it is impossible to distinguish any morbid changes in sections of the organ after death, except, perhaps, a little increase in the amount of fibrous tissue present.

In ordinary goitre—a disease which is not unknown in the Peak district, but which is seen to the greatest extent in the valleys of Switzerland, Italy, and elsewhere—the enlargement of the thyroid is often enormous. The swelling may fill up entirely the space between the summit of the thyroid cartilage and the sternum, and may reach up on both sides nearly to the angles of the jaws. The alteration need not affect the entire gland; sometimes only one lobe or the isthmus is affected, while the rest of the gland is unaffected.

The histological appearances constituting goitre are various. In some cases there is a dilatation of the follicles of the gland, which become filled with colloid, or sometimes with gelatinous material. The walls of the cysts may be lined with a fairly distinct layer of flat epithelium, but this epithelial layer may be completely wanting. At the same time the cysts may contain blood or degenerated blood. The cysts differ considerably in size, some being as large as a walnut, and others being quite microscopic. In other cases the gland is partly solid, and then portions are found which consist of cells with an alveolar arrangement, but with a complete absence of colloid or other secretory material. The blood-vessels may also undergo change, either undergoing a considerable increase in the thickness of their walls or becoming dilated and angeiomatous.

(3) The **degenerative** processes may occur in the case of the thyroid either in connection with the unaltered gland or in connection with antecedent morbid changes. Thus the hyaline and the myxomatous degenerations are fairly common, and although they are generally seen in combination with those alterations which go to form goitre, they may occur in the otherwise unaltered gland. Lardaceous disease has been found

in the thyroid arteries, both in the unaltered and in goitrous glands.

(4) **New-growths.**—The new-growths of the thyroid are partly non-malignant, partly malignant. Of the non-malignant growths the most important is an adenoma which frequently leads to a considerable increase in the size of the organ, and which is closely allied to the change that constitutes the cystic form of goitre. In it there is a formation of a number of irregular acini which are, for the most part, filled with colloid material. These acini are irregular by way of their sizes more than by way of their shapes. Speaking generally, they are of rounded shape, but the variation in size is considerable. Some of the acini form veritable cysts, while others are apparently identical in appearance with the acini of the normal gland. The tumours differ somewhat so far as their composition is concerned in different parts. Thus we may find that in one situation the cystic arrangement is marked, and the amount of colloid material is considerable, while the epithelium is flat and is often wanting in places. Close by, the acini may be small, with a very inconsiderable formation of colloid material, and with a lining membrane which consists of well-formed cells having round deeply staining nuclei and a large amount of protoplasm.

Malignant growths of the thyroid are far less common than non-malignant. They may be either carcinomatous or sarcomatous. In carcinoma there is generally the formation of irregular nodular masses of a whitish colour and soft consistency. The growths are generally confined to one portion of the gland, but since carcinoma for the most part arises in goitrous glands the rest of the organ is not normal. Histologically, the growth is a typical carcinoma of the spheroidal-cell variety, but sometimes the appearances are those of a columnar-cell carcinoma. The carcinomatous cells may undergo colloid degeneration, or there may be present in the centre of the acini or tubules of the growth a colloid-like material which is a representative of the normal secretion. When either of these conditions obtains, the appearances of the carcinoma may be very like those of a tubular non-malignant adenoma. The sarcomata of the thyroid are generally of the mixed-cell variety. They form whitish masses that are confined to one or more portions of the organ. Both sarcoma and carcinoma of the thyroid are associated with the formation of metastases in which the characters of the primary growth are reproduced.

SECTION XIV

THE URINARY ORGANS

ALTHOUGH many of the diseases of the generative organs affect portions of the urinary apparatus secondarily, it is more convenient to separate the two systems, and to indicate, where both systems are affected, the ætiological relations between the various morbid conditions concerned.

(1) THE KIDNEYS

(1) **Atrophy and hypertrophy.**—The usual size of the kidneys varies considerably even under normal conditions. As a rule, we may say that the kidney of a normal healthy male weighs about five ounces, but we frequently meet with organs which are apparently quite free from disease which weigh seven or even nine ounces. Nor can we associate the size of the kidneys, more than very roughly, with the size and build of the individual; the factors seem to be completely independent.

The commonest cause of atrophy of the kidney seems to be advancing age. The senile kidney is always relatively small. It is also the subject of a certain amount of fibrosis, but to that we shall have to refer later. Disuse atrophy is but rarely met with, and only in connection with some morbid condition of the ureters, whether congenital or acquired.

Hypertrophy is seen particularly when one of the two organs has become functionless, owing to either congenital or acquired disease. In the case of acquired disease the commonest condition upon which the hypertrophy depends is a disorganisation of the fellow kidney occasioned by the presence of a calculus.

(2) **Degenerative and infiltrative changes.**—The kidney is very liable to changes of this description. To all of them attention has been directed earlier, so that they will not call for detailed description here.

(*a*) **Cloudy swelling** (fig. 7) is more commonly met with in the kidney than in any other organ. The cortical substance has the characteristic boiled appearance, and consistently with this fact we find that the particular changes are principally evident in the cells of the convoluted tubules. Here, the cells are swollen, their protoplasm is granular, their outline is ill defined, but their nuclei are generally clear and stain well.

(*b*) Fatty degeneration also occurs in the renal epithelial cells with fair frequency. It occurs most commonly when the cells have become affected by some antecedent change of which the most important are inflammatory. Thus we find that the greatest evidence of fatty degeneration of the kidney is associated with the subacute inflammations. Under these circumstances the presence of a large number of fat globules leads to an alteration in the appearance of the organ. It becomes enlarged and white, so that the fatty change plays a great part in the formation of the 'large white kidney.' The fat globules are generally of small size, and it is the epithelium of the convoluted and irregular tubules that is particularly liable to be affected.

(*c*) The chief **pigmentary** changes to which the kidney is liable are those in which the bile pigments and iron are deposited. In the case of **bile** we may find that the deposit is in the lumina of the tubules, or it may be actually present in the epithelial cells themselves. In either case the material may be deposited in the form of granules, or it may lead to a diffuse staining of the epithelial cells or of the entire kidney. Frequently the epithelial cells which contain the pigment become desquamated, and then lie free in the lumen of the tube or become incorporated into casts.

The deposition of **iron** occurs under the same conditions as accompany the production of siderosis of the liver. The iron is, however, less frequently deposited in the form of granules in the case of the kidney. Far more generally the renal epithelium is diffusely impregnated, so that the organ assumes a uniform greenish-blue colour when treated with potassium ferrocyanide and hydrochloric acid, even though examined with high powers of the microscope. A certain small amount of iron is, however, present in the granular form.

The only other pigmentary deposit that need be mentioned is **silver**. Argyriasis is at the present time a rare condition, but when it occurs it is usual to find that there is a deposit of fine granules of silver in the epithelial cells of the renal tubules.

The kidneys are very commonly the seat of the **lardaceous** change when this occurs in anything more than a slight degree. The first parts to be affected are the small vessels of the glomerular tufts. Unstained, or stained in an indifferent manner, the tufts then show the presence of a number of colourless translucent masses or slightly tinted masses, as the case may be. In an early stage these masses may easily be overlooked, unless the special staining with methyl violet be resorted to, but then the character of the change becomes manifest. At a later stage the whole of the tuft becomes modified. At the same time it appears to be larger than it was before, and nearly fills the Bowman's capsule. The change, too, passes to the arterioles that supply the tufts, and then it is clearly to be seen that it is the middle muscular coat, both as concerns its circular and its longitudinal fibres, that is affected. The renal substance, apart from the blood-vessels, is always profoundly affected in lardaceous disease of the kidney. In a large number of cases the changes are those dependent upon a tubal nephritis which the organ has undergone from being less resistent than normal. In other cases the changes consist principally in a fatty degeneration of the renal epithelium with its desquamation into the lumina of the tubules. These changes need not be described here, for they will call for attention later. It is extremely rare for the lardaceous change to be associated with fibrosis, and when such an association does occur it must be looked upon as accidental.

A form of deposition to which the kidneys are liable is that in which the deposit consists of some substance which is derived from the urine. Thus we may find that the collecting tubules are the seat of a deposit of uric acid or of phosphate of calcium, or sometimes of oxalate of lime. These changes are closely akin to those which culminate in the formation of urinary calculi. To the latter subject we shall return later, but the question of deposition of granules of the various salts may be dismissed here. Of all the deposited materials of the kind under consideration, the one most generally met with is **uric acid**. It occurs under two conditions. We may either meet with it in gouty persons, and then it is found in the form of a dead-white deposit arranged in lines running alongside the tubules in the medullary portion and, to some degree, as isolated points in the cortical portion of the organ. In these cases the material is in reality a biurate of soda, and is present in the form of delicate needles ; the condition is exactly comparable to the formation of the 'chalk stones' in the neighbourhood of the joints of the hand, or the deposition of the salt in the articular surfaces of the joints themselves. In the other case the material is of a bright yellow or brown colour, and has a similar arrangement, but appears to consist of uric acid itself, and is found in the kidneys of new-born infants. The condition is known as **uric acid infarction**. It is not very frequently seen, and only in the case of infants of a few days old at most. The material is present in a semi-crystalline form, and is found in the lumina of tubules which are dilated above. A very common situation for the deposit is the apex of the urinary papillæ. The kidneys which are the seat of uric acid infarction do not usually manifest any other change.

(3) **Vascular changes which are non-inflammatory.**—Under this heading we have to consider cardiac changes, infarction, and the appearances met with in leuchæmia.

(*a*) **Chronic venous congestion.**—This condition is principally seen in cases of cardiac failure. When the tricuspid valve becomes incompetent and the entire systemic venous area becomes engorged, the veins and capillaries of the kidney become distended with blood also.

Macroscopically, the cardiac kidney is somewhat larger than normal, and much redder and firmer. The capsule is generally somewhat adherent, and when it is stripped off, a portion of the subjacent renal substance is removed at the same time. This adherence of the capsule does not, however, always obtain. The stellate veins are obviously fuller of blood than normal, and stand out as well-defined lines, directly the capsule has been removed. At the same time it is probable that the congestion will be manifested by the large amount of blood that drips from the surface when the organ is divided in the usual way with the knife.

Microscopically, the evidences of congestion are considerable. The vasa recta are full of blood, and the same is true of the capillaries constituting the Malpighian tuft. In the latter case we may find that actual rupture has taken place with the result that blood is present in the space between the layers of Bowman's capsule. It is not unlikely, too, that a certain amount of blood may be present in the urinary tubules, and sometimes this is the case to so marked an extent that blood casts of the tubules are formed.

In addition to the signs of congestion, it is common for the kidney to contain a larger amount of fibrous tissue than normal. This is distributed throughout the organ with fair evenness, and is not generally present in considerable quantity. It is owing to the presence of an abnormally large number of strands of fibrous tissue passing between the cortex of the kidney and the capsule that an attempt to remove the capsule leads to laceration of the surface of the organ. To some degree the contraction of the fibrous tissue produces changes in the renal elements themselves. The wall of Bowman's capsule becomes thickened, and the glomeruli themselves become smaller in size. Sometimes, however, the fibrous tissue, by its contraction, completely obstructs the lumen of a tubule close to the glomerulus; under these circumstances either the glomerulus may become itself converted into a mass of fibrous tissue, or the tuft may atrophy and the capsule itself become converted into a cyst. Cysts, indeed, are fairly common in cases of cardiac kidney, though not so common as in certain other chronic changes of the organ. There is reason to believe, however, that they are not always formed from glomeruli, but that they may be formed from portions of tubules that have been constricted above and below.

The reason for this formation of fibrous tissue in the cardiac kidney is not clear. Nor is the fibrous tissue always present in excess. Such is, however, generally the case, and we must probably correlate the change with the chronic venous congestion, as we have to do in other cases, without attempting to give an explanation.

(*b*) **Infarction** of the kidney is a change which it is difficult to either include or exclude from this class or the class of inflammatory processes. Where the embolus which occasions the infarction is septic, it is clear that the subsequent changes are inflammatory, and they will be considered under that heading. When the infarction is aseptic, the amount of inflammation is so small that it may practically be neglected, although, as will be seen, evidences of this inflammation are not wanting.

Renal infarcts are of either the anæmic or the hæmorrhagic variety, and of these anæmic infarcts are far the more common. It is, indeed, practically only in the case of very small infarcts that the hæmorrhagic form is seen.

Anæmic infarcts of the kidney may be so large that they involve as much as a third or a half of the entire organ. This occurs when the embolism upon which the infarction depends implicates a main branch of the renal artery. More commonly the infarcts are about the size of the thumb-nail. The centre of the infarct is of a dead yellowish-white colour, but at the margins there is a narrow zone of deep congestion which is fairly sharp towards the infarct itself, but shades off towards the still normal kidney substance. The infarcted area is flush with or a little lower than the general level of the organ, and the broadest part of the infarct is situated on the surface.

Microscopically, the changes to be noticed in an infarct of the kidney are principally those of the congested area which bounds it. In the infarcted region itself the general renal structure is but little different from that of the normal tissue outside, particularly if the infarct be very recent. If it is a little older, we shall find that the nuclei fail to stain with their normal distinctness, so that on holding the section up to the light it is possible to see that even in the stained microscopic section the area of infarction is easily recognisable. Indeed, one of the best ways of understanding the histology of an infarct is to orient oneself from time to time by examining the section with the naked eye. In the zone of congestion, it is seen that the capillaries are distended with blood and that hæmorrhages have taken place at various points, bursting, at times, into the tubules and there forming complete blood casts.

In course of time, assuming that the embolus is aseptic, the dead tissue in the infarcted area undergoes absorption and the potential lacuna is filled up by newly formed fibrous tissue. Hence the infarction becomes replaced by scar tissue, and this, owing to its contraction, causes the former seat of the infarct to be represented by a depressed cicatrix on the surface of the organ.

In the case of the much rarer hæmorrhagic infarct the appearances are obscured by the large amount of blood which lies within and without the vessels of the infarcted area. Remnants of the renal substance are recognisable, but they are much broken up. Assuming that the infarct follows a normal course, it will end in the formation of a depressed scar similar to that which terminates an anæmic infarction. In a large number of cases, however, the infarction is hæmorrhagic because it depends upon the impaction of an intensely septic embolus. When this is the case the ultimate fate of the infarcted area is determined by this fact.

(*c*) **Pseudo-leuchæmia.**—In pseudo-leuchæmia it is not uncommon to meet with masses of leucocytes in the solid organs and particularly in the spleen, liver, and kidney. In the kidney these masses are of a white colour and are easily recognisable by the naked eye. The foci are generally so definitely circumscribed that they simulate secondary nodules of a malignant growth. They are rarely very large, and under the microscope they are seen to consist of numbers of leucocytes. As to the nature of the leucocytes this differs in different cases. Occasionally we find on appropriate staining that the cells are finely granular oxyphil cells in which the granules are well marked, in other cases they appear to be lymphocytes. Although the foci seem to be so definitely circumscribed when viewed by the naked eye, they gradually shade off into the general tissue of the kidney.

(4) **Inflammatory changes.**—The kidney is very liable to be the seat of inflammatory changes. Some of these are acute, some subacute, some chronic, some are definitely associated with the presence of micro-organisms, but in all of them it is customary to find that the entire organ is affected, in spite of the fact that in many instances the disease seems to be localised more or less completely. From this it follows that, although it is convenient to divide the various inflammatory changes in the kidney according to the most characteristic feature of the inflammation, it is not strictly accurate to distinguish a glomerular nephritis, for example, from a tubal nephritis or an interstitial nephritis. For the same reason the differentiation of the renal inflammations into parenchymatous and interstitial is unsatisfactory.

(*a*) **Glomerular nephritis.**—In certain cases, notably those which occur in connection with the commencement of scarlatina, the kidney becomes affected by an intensely acute inflammation which expends itself principally upon the glomeruli. The capillaries composing the tufts become distended with blood to such an extent that the tuft fills the capsule almost completely. At the same time hæmorrhages into the space between the tuft and Bowman's capsule are very common. The rest of the organ appears to be normal beneath the microscope, but to the naked eye it is manifestly redder than normal and swollen. Sometimes, indeed, the congestion is so considerable that the capsule becomes torn, and when a section is made into the organ in the ordinary way, there escapes so large a quantity of blood that it drips from the surface. In a pure form this variety of nephritis is not often seen, but a certain amount of glomerular affection is common in all the more acute varieties of inflammation. The degree of congestion and the degree to which the glomerular affection enters into the entire change are, in fact, a measure of the acuteness of the nephritis.

(*b*) **Tubal nephritis.**—In some cases the renal tubules are affected to so considerable an extent that the changes in them dominate the whole picture. It is chiefly in the proximal and distal convoluted tubules and in the irregular tubules that the alterations occur, but the remaining parts of the renal unit do not escape. It is the tubal variety of nephritis which constitutes the so-called parenchymatous nephritis.

The macroscopic change consists in an enlargement of the organ which especially concerns the cortical portion. This enlargement varies considerably according to the date at which the patient succumbs after the onset of the renal disease and according to the exact nature of that disease.

So far as the date after the commencement of the affection is concerned at which the organ is obtained, the kidney is paler the later this is, owing to the changes which go on gradually in a kidney of which the tubules have become altered by inflammation. These changes consist partly in a diminution of the congestion, and partly in an extensive fatty degeneration of the altered renal epithelium.

Four distinct varieties of tubal nephritis are to be recognised. First, there is a class in which the inflammation is acute, in which the organ was previously healthy, and in which the organ is obtained soon after the commencement of the disease. In this class the kidney is somewhat enlarged, bright red, smooth on the surface, and the capsule strips with abnormal ease. Second, there is a class in which the inflammation is subacute, in which the organ was previously healthy, and which does not occasion the patient's death till somewhat later. In this class the kidney is greatly enlarged, white, pale, or mottled in colour, the capsule strips with abnormal ease, and leaves a smooth surface upon which the injected stellate veins show up with great distinctness. Third, comes a class which arises out of the two previous, in which the nephritis is receding and in which the organ is obtained at a still later date after the commencement of the illness. Here the kidney is enlarged, but not so greatly as in the second class, and more than in the first. It is pale in colour, its capsule strips off with some difficulty, and frequently tears off a portion of the cortical renal substance with it, or, if this does not occur, leaves a granular surface beneath. In this class the organ was also previously normal. The fourth class comprises a group in which the kidney was the seat of chronic fibrosis before the tubal inflammation occurred. In it we have a combination of the two changes, so that the organ is about the normal size or a little enlarged, is granular on the surface, is somewhat pale in colour, and possesses the particular changes characteristic of chronic renal fibrosis, in addition to inflammatory changes in the tubules. These classes may respectively be known as (α) Acute tubal nephritis, (β) Subacute tubal nephritis or large white (or mottled) kidney, (γ) Contracted white kidney, and (δ) Nephritis secondary to chronic fibrosis.

The microscopical appearances of these different classes are themselves quite different, and need to be considered separately.

(*a*) In **acute tubal nephritis** the evidences of congestion are marked in the small vasa recta and the capillaries that traverse the organ, and actual hæmorrhages are common. The glomeruli are generally fairly normal in appearance, except so far as they share in the general congestion. Great changes are visible in the convoluted tubules. The epithelial cells are large and swollen, their protoplasm is granular, their nuclei are indistinct (thus

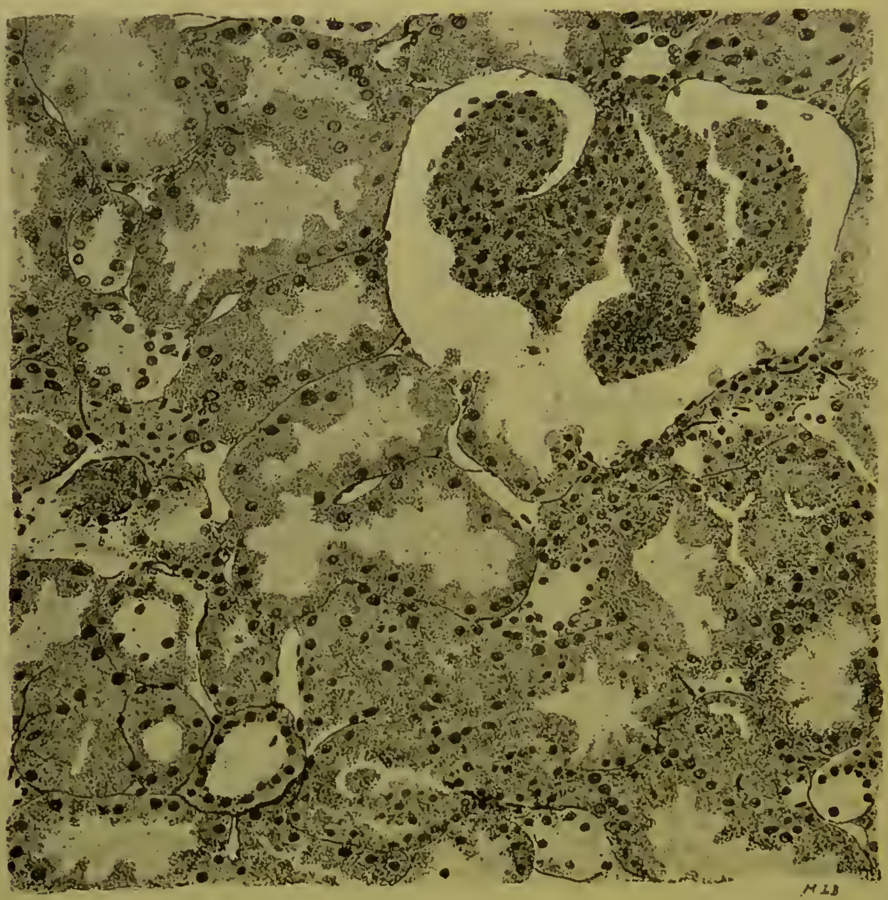


Fig. 126.—Section of Kidney showing Acute Tubal Nephritis. × 500.

The glomerular tuft is not greatly altered; but much of the lining endothelium of Bowman's capsule has disappeared. There is very little solid material in the space between the tuft and the capsule. The convoluted tubes show swollen granular and irregular epithelium, which has in some places desquamated; the nuclei of the cells are pale, and in many places wanting. The lumina of the tubes are filled with granular material (precipitated proteid), and often the outline is indistinct. The straight and collecting tubules are similarly but not so extensively affected. The amount of fibrous tissue through the section is not increased. This figure should be compared with fig. 7.

differing from the nuclei in cloudy swelling), the size of the lumen is greatly diminished, many of the epithelial cells are desquamated, and the lumen of the tubule may be blocked by casts that may consist of blood or of epithelial cells, or of coagulated proteid derived from the inflammatory exudation. The remaining elements of the organ, and particularly the conducting, the collecting, and the straight tubules, are apparently little altered or not affected at all.

(β) In **subacute tubal nephritis** the evidences of congestion present in the first class of case are entirely wanting. The glomeruli are frequently larger than normal, and there is an increase in the number of nuclei which stain deeply with the ordinary nuclear stains. These are possibly nuclei of leucocytes, but possibly also of proliferated connective-tissue cells of the glomerular vessels. The principal seat of change lies in the convoluted tubules. Here the epithelial cells are swollen and granular, their outlines are indistinct, their nuclei have disappeared in many cases, and those which remain take the stain very badly, and the cell protoplasm shows the presence of a number of fat globules of varying, but mostly small, size. The lumina of the tubules are not only small, owing to the encroachment upon them of the swollen epithelium, but are also, in the majority of cases, blocked by casts composed of blood or epithelial cells or granular material or a combination of these substances. The principal constituent of the casts in this form of nephritis is desquamated epithelium. In the mottled form of the disease there are usually some small evidences of congestion. It must be remembered, however, that the macroscopic evidences of congestion are far greater than the microscopic, owing to the large amount of blood which is removed from the mass of tissue during the processes of preparation.

(γ) In **contracted white kidney** the tubal changes are associated with a general increase in the amount of interstitial fibrous tissue throughout the organ. This fibrous tissue originates in connection with the pre-existing fibrous stroma of the kidney, and is an evidence of the retrogression of the inflammatory process. Hence the newly formed fibrous tissue in this variety of nephritis is of a definitely cicatricial type. In an early stage the change is characterised by the presence of a large number of fibroblasts along the lines of the pre-existing fibrous tissue. Sometimes there is a certain accumulation of leucocytes in the same situation, but this is only at a very early stage, and is not very common or conspicuous. As the fibroblasts form fibrous tissue, the amount of interstitial fibrous tissue increases, and the number and size of the individual tubules diminish. At the same time the fibrous tissue contracts, leading to the granular appearance of the surface of the organ and the adhesion of the capsule to the cortex. The contraction of the fibrous tissue is also answerable for the formation of cysts in the organ, although these are not usually so numerous or so large as in the chronic fibrotic kidney. The fibrous tissue is distributed with fair evenness throughout the organ, and is always very noticeable in the pyramidal portion.

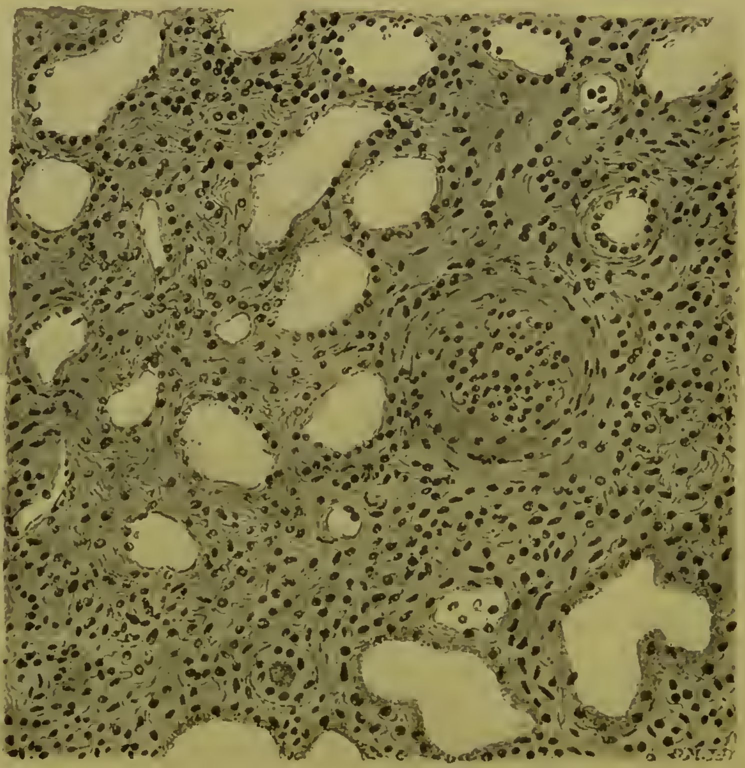


Fig. 127.—Section of Contracted White Kidney. × 420.

The striking features are an enormous increase in the amount of fibrous tissue, and the cystic dilatation of many of the urinary tubules. Towards the centre is a glomerulus which is obliterated, and has become converted into practically a mass of fibrous tissue. The renal epithelium is fairly well marked though flattened, the nuclei are distinct, and there is an absence of precipitated proteid in the lumina of the tubules. The greater number of nuclei present in the solid portions are those of young connective-tissue cells. From the body of a young woman who died eleven months after presenting symptoms characteristic of acute tubal nephritis.

The tubal changes do not call for special mention, for they are identical with those obtaining in the subacute variety of tubal nephritis. The only difference lies in the fact that there is generally evident a greater amount of cell desquamation, partly by the presence of epithelial casts in the tubules, and partly by the existence of numbers of tubules which are lined by no layer of epithelium at all. Congestion is practically absent, a fact which is largely dependent upon the contraction of the fibrous tissue. This absence of congestion, coupled with the large amount of fatty degeneration which has been undergone by the renal epithelium, explains the pale colour of the organ. For a reason that will appear later it is important to note that the renal arterioles do not suffer any notable changes in their walls.

(δ) In **nephritis secondary to chronic fibrosis** we have a combination of the changes characteristic of tubal nephritis and those characteristic of chronic fibrosis. To the latter it will be necessary to refer in detail later. With regard to the truly inflammatory changes, it need only be said that they may present evidences of being either acute or subacute. It is always the tubules that are chiefly affected, the glomeruli rarely showing any inflammatory changes at all. The amount of congestion varies considerably, but is usually more marked than in either the large or the contracted white kidney. Hence it comes about that many of the cases belonging to this class have a somewhat mottled appearance, and from this fact they are sometimes spoken of as 'small mottled' kidneys. The entire change is not an uncommon one, owing to the prevalence of chronic fibrosis of the kidney and the fact that an organ thus altered is particularly liable to be the subject of inflammation because of its diminished powers of resistance. Histologically, this class of nephritis is very liable to be confounded with the contracting white kidney, but a differentiation between the two can generally be made by paying attention to the presence or absence of the vascular changes which characterise chronic renal fibrosis.

(*c*) **Consecutive nephritis.**—This variety of inflammation of the kidney is acute, but it differs from acute nephritis, as it has been described above, in the fact that it is not a primary renal condition, but depends upon an extension of an inflammatory process from the bladder by way of the ureters.

The change shows itself in two chief forms. In the first, which is the more acute, the kidney is enlarged (particularly the cortex), and swollen; it is of a pale colour, with streaks of red on the cut surface corresponding to the vessels, and a general turbid appearance. The capsule strips easily, provided that the organ has not been the subject of an antecedent chronic fibrosis. Frequently the pelvis is thickened and the calyces are larger than normal, while the apices of the pyramids are flattened and do not project so far into the calyces as normal. Points of pus may be present in the cortical or medullary substance. In the second variety the organ is converted into a bag of pus which is generally considerably larger than the normal kidney. The wall of the bag is perhaps not more than a quarter of an inch in thickness, and there is no differentiation into cortical and medullary substance, or any evidence of calyces and pelvis. In fact, the pelvis is enormously dilated and is almost in direct contact with the capsule of the organ. Between these two extremes all forms may be found. The first form is generally termed 'consecutive nephritis,' the second is often known as 'surgical kidney.'

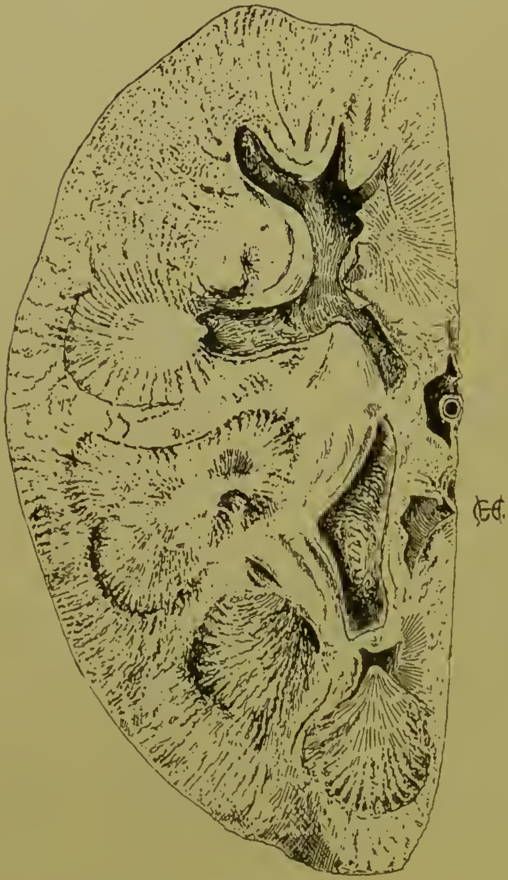


Fig. 128.—Consecutive Nephritis. × $\frac{3}{4}$.

From a case in which there was prostatic enlargement. The organ is enlarged and pale, with lines of congestion running radially in the pyramids and the cortex. These lines are those of the inflamed vasa recta. The lining membrane of the pelvis and calyces is thickened.

A condition which lies somewhat between the two above, but which does not merit a separate name, is that in which the foci of pus which are found in the early stage of consecutive nephritis are sufficiently large to constitute definite abscesses. These may be present in so large numbers, and may be individually of so considerable size, that they may ultimately become incorporated in the cavity of the distending pelvis. That is to say, a surgical kidney may be the result of two slightly different processes.

Microscopically, the kidney is the subject of the most profound alteration. In the earlier stage the fact that we have to do with renal substance is recognisable, although the epithelium of the tubules is often entirely disorganised. But in the case of a fully developed surgical kidney it may be impossible to find even the smallest trace of renal substance. In addition to the disorganisation of the epithelium, the interstitial connective tissue shows the effects of inflammation in the presence of a number of leucocytes. The degree to which this infiltration of leucocytes takes place varies greatly; as a rule, it is not very considerable, except at those spots at which the cells collect in sufficient numbers to constitute an abscess. The glomeruli share in the general disorganisation, but since the true renal substance is affected in a direction from the pelvis to the cortex (in which the glomeruli are situated), they are apt to be modified somewhat late in the disease. The epithelium-lined pelvis is always the seat of change. The epithelium itself undergoes proliferation in places, and, in places, desquamates. It is always congested and rough on the surface and, as the result of the inflammation, is always thickened. If the case has been accompanied by an alkaline condition of the urine, as is common, there may be a deposition of calcium and magnesium phosphate upon its surface. The condition as such is not accompanied by any new formation of fibrous tissue.

Microscopic examination of the wall of a surgical kidney is very unsatisfactory. As a rule, little more than a somewhat degenerated fibrous tissue is found which shows an increase in amount and the presence of a number of leucocytes. True renal elements are practically absent.

(*d*) **Pyonephrosis.**—Under this name, which is essentially clinical, are included most of the conditions in which the kidney is the seat of a suppuration which has proceeded to a sufficient extent to convert the kidney entirely or in large part into a bag of pus. In the majority of cases this has depended upon the extension of an inflammation of the pelvis, so that the principal causes of pyonephrosis are renal calculus and diseases of the lower portions of the urinary tract, which have induced secondary renal changes. As will be seen later, tuberculosis of the kidney is a condition which in a strict pathological sense cannot be separated from the suppurative conditions which are induced by the ordinary pyogenetic cocci. Nevertheless it is not customary to speak of a tuberculous nephrosis as being a pyonephrosis. The same is true with the abscesses that are liable to be formed in the kidney in the course of pyæmia. The changes met with in tuberculosis, and along with renal calculus, are sufficiently distinctive to merit separate description, and we shall consider them later, but a few words may be said with regard to pyæmic abscesses in the present place.

Pyæmic abscesses are always the result of the lodgment of a septic embolus in the kidney. When the embolus becomes lodged, it leads to the formation of an infarct of the ordinary kind, anæmic if the embolus is large, and hæmorrhagic if it is small. It must be noted, however, that the tendency to the formation of hæmorrhagic infarctions is greater when the embolus is septic, owing to the greater intensity of the irritant. Into the subsequent changes which lead up to the formation of the abscess it is unnecessary to enter.

Pyæmic abscesses in the kidney are generally of small size; in fact, in a large number of cases they are microscopic. Sometimes, however, they reach to a considerable size. The number which will be found varies, but is rarely great. In the process of extension of the abscess neighbouring parts are liable to be involved. Thus an abscess in a pyramid may extend into the pelvis of the kidney, and induce a suppurative pyelitis, and one in the cortex may extend beyond the capsule and induce a suppuration in the perinephritic cellular tissue the limits of which are likely to be very wide.

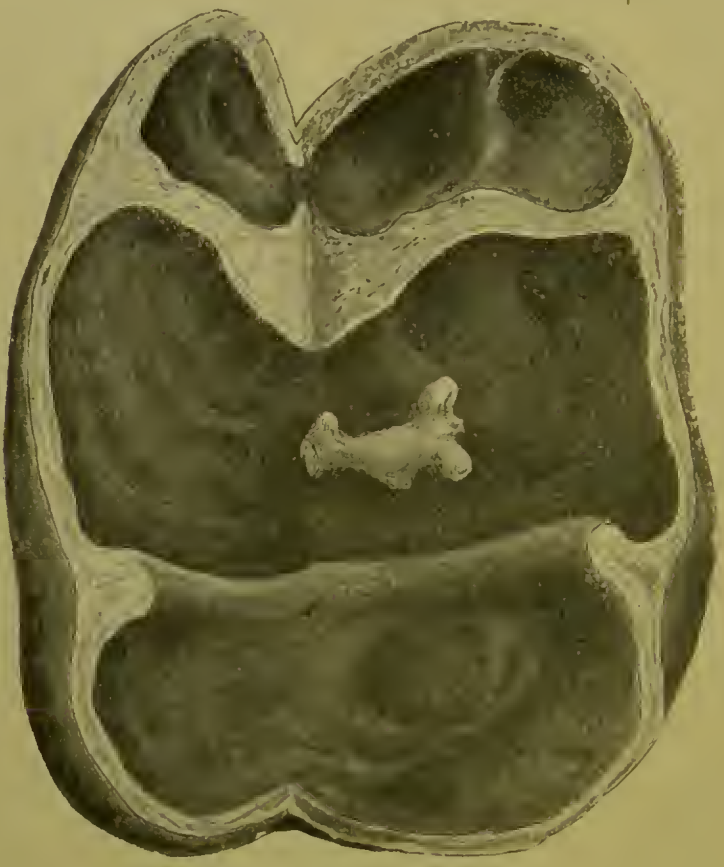


Fig. 129.—Calculous Pyonephrosis. × $\frac{3}{4}$.

Owing to dilatation of the pelvis, the organ has been converted into a large sac with smooth walls that consist of little more than fibrous tissue. In the pelvis is the branched uric acid calculus which occasioned the change.

(*e*) **Tuberculosis.**—Tuberculosis shows itself in the case of the kidney in two forms. It may either be a special part of a general infection, and then the tubercles are miliary and may not even have caseated in the centres, or it may be a special infection which is primary in the kidney or in some other part of the genito-urinary tract. With regard to the first variety it is unnecessary to speak.

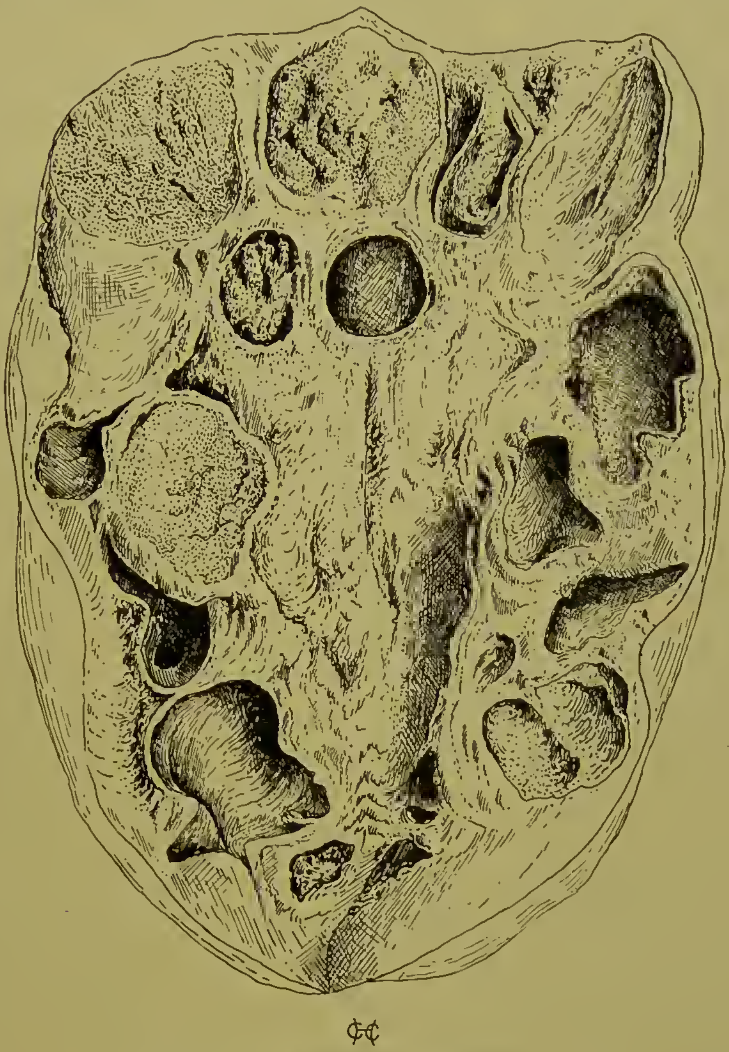


Fig. 130.—Tuberculous Kidney. × $\frac{2}{3}$.

The organ is enlarged, and numerous cavities with thick walls are present in various parts. The pelvis is notably thickened. Very little of the original structure remains.

When the tuberculosis is primary in the kidney, or occurs there as the result of an extension of the process from some other part of the genito-urinary tract, the changes in the organ are profound. The condition no doubt commences by the deposition of miliary tubercles, but it rapidly passes on to the formation of large caseous masses. Hence the characteristic feature of tuberculosis of the kidney of this kind is the presence throughout the true renal substance of a number of softening caseous foci. When a section is made into the organ, this caseous material escapes readily, owing to its fluidity, and a number of cavities are left which are lined internally by a thick curdy material. These cavities are liable to be found anywhere in the organ, and by a process of extension they open into one another and into the pelvis, so that ultimately the kidney becomes converted into a loculated cyst in which the former pelvis can only be recognised by its situation. The pelvis itself is thickened and lined by a layer of yellowish curdy material similar to that present in the cavities of the kidney itself. Little, if any, unaltered kidney substance can be discovered in an advanced case, while the general result of the disease is an enlargement of the organ. The fluid contents of the cavities chiefly consist of broken-down caseous material, but a large number of pus cells of the ordinary kind are also present. Hence the urine contains a large amount of pure pus in cases of advanced tuberculous disease of the kidney.

Other inflammatory diseases of the kidney may practically be neglected, so rarely are they met with. Syphilis is the commonest of them, but gumma of the kidney is very rare, and presents no special features that call for remark.

(5) **Chronic fibrosis.**—The chronic fibrotic kidney is known by other names, of which the 'contracted granular,' 'red granular,' 'small red,' and 'arterio-sclerotic' are the commonest. The organ is always diminished in size, and sometimes the diminution is sufficient to reduce the weight of the pair of organs to half the normal of one. The surface is granular, and as a rule the granulation is of a fine kind. The capsule is adherent, and frequently it is impossible to strip it off in its entirety, even though one pay no attention to the portions of cortex which are removed at the same time. The cortex is diminished in thickness, and this is one of the most characteristic features of the condition; it is also common to find that there are present in it numbers of small cysts with clear watery or gelatinous contents of a colour that varies between a pale straw yellow and a reddish brown. Partly as the result of the diminution in size of the organ and partly, perhaps, owing to a definite new formation, the amount of fat in the hilum of the kidney is greatly increased. The amount of fibrous tissue throughout the organ is increased, in well-marked cases, to a macroscopic extent, and the arterial walls are much thickened as the result of an alteration in their middle coats, so that they stand up rigidly on the surface of a cut section and maintain their orifices widely open. The colour of the kidney is

a deep red, but if it has become the subject of tubal nephritis it may be mottled, as has already been said.

Microscopically, in such a well-marked case, it is seen that the organ is entirely altered as the result of a large new formation of fibrous tissue which is distributed fairly evenly through the cortex and medulla. The increase in the amount of fibrous tissue shows itself in a very characteristic manner by the great thickness of Bowman's capsule. This is frequently three or four times as thick as normal, and since the change is either completely absent or is but slight in other conditions in which there is an increase in the amount of fibrous tissue in the kidney (e.g. the contracted white kidney), it affords a valuable means of distinguishing the chronic fibrotic kidney from other varieties of chronic renal change.

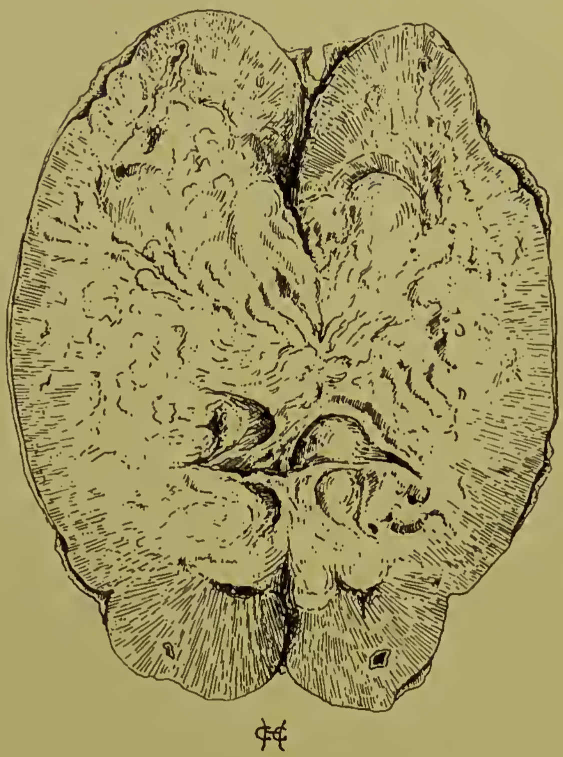


Fig. 131.—Chronic Fibrosis of Kidney (Chronic Granular Kidney). Natural Size.

The edge of the cut section is irregular, and the cortex is diminished in thickness. Very little of the pelvis is visible, its place being largely taken by a considerable mass of fatty tissue. The pyramids are not recognisable in the drawing, but they were much atrophied; in fact, the kidney consisted of a central mass of fat surrounded by a narrow zone of renal tissue.

The amount of fibrous tissue varies very considerably. In the simplest form of chronic fibrosis—namely, that which accompanies old age—the amount is small, though definite, but in a really advanced condition which is quite outside the pale of normality the amount may be very considerable. It is never so great, however, that it becomes impossible to distinguish the fact that the tissue under observation is kidney.

The contraction of the fibrous tissue occasions another characteristic appearance of the chronic fibrotic kidney. This is the irregularity of the size of the tubules. Owing to the fact that they are obstructed at various points, many of the tubules become dilated. In some cases this dilatation proceeds to the formation of those cysts to which attention has already been directed, but in any case the general result is a marked irregularity of the diameters of the tubules, particularly those in the cortex. In the medullary portion the amount of fibrous tissue present is as great as it is elsewhere, but the effect of the contraction is not so much shown by the formation of cysts as by the complete removal of a large number of the tubules owing to pressure atrophy.

The vascular changes are well marked in the case of the arterioles and consist, as has been said, in an increase in the thickness of their middle coat. This change is principally one of fibrosis, but apparently the muscular fibres also increase in size and in number. The minute vessels composing the Malpighian tufts also undergo change, in many cases becoming completely converted into fibrous tissue. These fibrotic glomeruli are much smaller than normal, and, unless care be taken, may escape notice altogether.

Quite apart from the glomerular change that has been mentioned above, the glomeruli in chronic fibrosis of the kidney are always shrunken. As a result, there is always an abnormally large space between the tuft and Bowman's capsule itself. This space is generally quite empty, but it may hold a small amount of granular material. Except in the rare instances in which a granular kidney becomes affected by an intense inflammation which involves the glomeruli, the space between tuft and capsule never contains blood.

It may now be mentioned that we have examined a variety of changes which are often spoken of collectively as 'Bright's disease.' Under this name are included several different conditions which are accompanied by the presence of albumin in the urine, and which were first described by Dr. Bright, of Guy's Hospital. From the common standpoint of the fact that the existence of albuminous urine is characteristic of the cases, 'Bright's disease' forms, more or less, a clinical entity. But there is no doubt that even amongst the cases originally described by Bright several different pathological conditions were included. Thus, although the greater number of his cases were examples of what we should at the present day term acute and subacute tubal nephritis, whether attacking previously healthy or previously fibrotic kidneys, a certain number were cases of lardaceous disease. The matter became still more complicated when the view was adopted that chronic fibrosis of the kidney, a disease in which it is common to find a small trace of albumin in the urine, is a chronic inflammation of the organ. For then a distinction was made between 'acute Bright's disease' (acute and subacute tubal nephritis and glomerular nephritis) and 'chronic Bright's disease' ('chronic interstitial nephritis' or, as it has been termed above, chronic fibrosis of the kidney). Owing to the confusion that was thus introduced, the term is now but little used, and when it is used its significance is only that a disease is present which is accompanied by albuminuria and is occasioned by organic changes primary in the kidney.

(6) **New-growths.**—The new-growths of the kidney constitute one of the most difficult chapters in the description of the neoplasms. Non-malignant tumours are not common and are of relatively little importance, but it is when we come to consider the malignant new-growths that the difficulties arise. From the fact that the kidney is a mesoblastic tissue, one might suppose that the malignant growths of the organ would be sarcomata exclusively. But this, as we shall see presently, is by no means the case.

The non-malignant growths are generally of inconsiderable size, not often exceeding that of a filbert or walnut. They are very rarely met with, but of them the fibroma and the lipoma seem to be the most common. Adenomata are also occasionally found, and they may be either of the alveolar or the tubular type. Intra-alveolar papillary growths are common in this variety of tumour. Adenomata met with in Cortex. Fibromata met with in medulla.

Of malignant new-growths which are secondary it is unnecessary to speak. No difference distinguishes them from secondary growths elsewhere. They may be either sarcomatous or carcinomatous.

Primary malignant new-growths occur both in childhood and in adult life. Of the growths which occur in childhood, a considerable number appear to be congenital, although the principal growth occurs after birth. This is particularly the case with those renal tumours which destroy life in children of less than two years. Such tumours as these are almost always sarcomata, but the actual nature of the sarcoma is frequently difficult to make out. The reason of this is that the composition of the tumour differs at different spots. At one, it may be apparently a simple small round-cell sarcoma, at another a large round-cell, and at yet another a mixed-cell sarcoma. Moreover, in a certain number of cases we find that striated muscular fibres are present, so that the growth has to be regarded as a rhabdomyosarcoma.

In adults the growths may be sarcomata having the varied characters which have been mentioned, but also we meet with growths that have close analogies with the carcinomata. As to the actual nature of these growths there is a difference of opinion. Some authors regard them definitely as columnar-cell carcinomata, and since there is a general tendency among growths of this description to present intra-alveolar papillary growths, they speak of them as **villous columnar carcinomata.** On the other hand, the growths have great resemblances to the cystomata of the ovary, which also frequently show the presence of intracystic

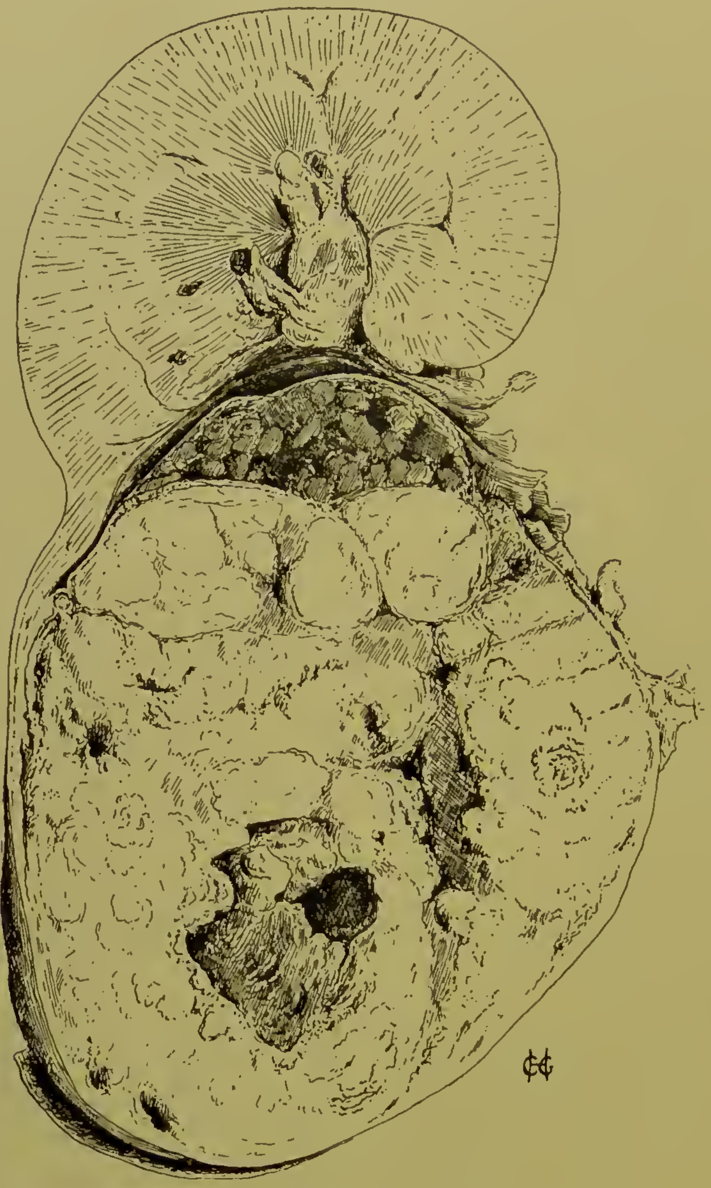


FIG. 132.—SARCOMA OF KIDNEY. × $\frac{2}{3}$.

The lower portion of the organ is replaced by a sarcomatous mass. This has not extended beyond the capsule of the organ, but over a portion of the convexity has expanded the renal cortex over itself. For the most part the growth, however, has replaced the renal substance.

papillary growths. Hence some authors prefer to speak of these renal tumours as **papillary cystadenomata.**

These growths are generally of considerable size. They affect a large portion of the kidney, either about the hilum or at the lower end. In part they replace the renal tissue by a process similar to that which obtains in the case of the malignant growths generally, but in part they simply displace it, and lead to a pressure atrophy with the production of a thin bordering of renal tissue around the tumour. They resemble the malignant growths generally in the fact that it is common for secondary growths to be formed elsewhere in the body, notably in the liver. For this reason it is preferable to regard them as carcinomata.

The histological appearances of these new-growths have largely been given above. It will therefore suffice to say that the sections show the presence of a number of cysts that are more or less filled with intracystic papillomata. These papillomata consist of a central connective-tissue supporting substance, and are covered by a layer of very delicate and regular columnar cells. The secondary growths have similar appearances.

New-growths of the kidney are very liable to undergo degenerative changes, of which the fatty change is the commonest. Frequently degeneration is accompanied by hæmorrhage into the centre of the growth, so that when a portion of the liquefied central material is examined, the nature of the tumour is quite indeterminable. This fluid material often, also, contains crystals of cholesterin which are found floating on the surface when the fluid escapes.

A form of growth occurs in the kidney which is characterised by the presence of the large cells that are met with in the cortical portion of the suprarenal body. The actual nature of these growths is very difficult to determine, but that they are malignant there is no doubt. It is generally considered that they originate in suprarenal ‘ rests.’

(2) THE PELVIS OF THE KIDNEY AND THE URETERS

The pathological conditions which affect the renal pelvis and the ureters are of importance in that they form a part of processes that have either originated in the kidney and have passed downwards, or have originated in the bladder and have passed upwards. In any case they are identical with conditions that have been or will be considered more fully elsewhere.

Although it is not common for a ureter or a renal pelvis to be affected independently, it is quite common for the pelvis and the ureter on one side of the body to be diseased while the other side is normal or comparatively normal. This, however, can only occur when the disease has passed from the kidney downwards. When the primary disease has been in the bladder or below, it is invariable to find that both sides are affected, though one may be more diseased than the other.

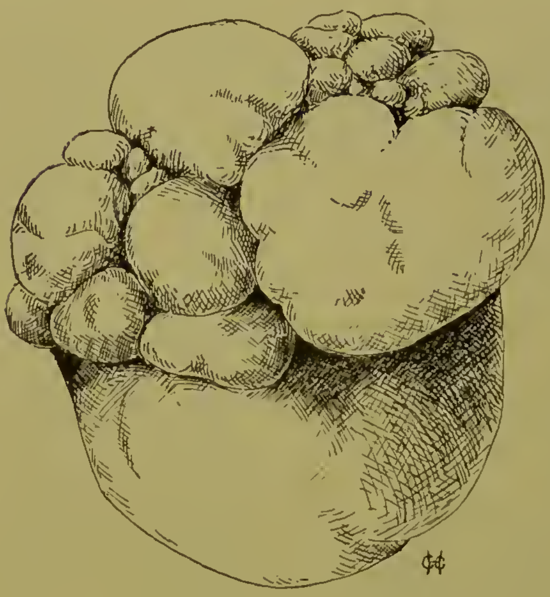


FIG. 133.—HYDRONEPHROTIC KIDNEY, FROM A CHILD. × $\frac{3}{4}$.

The organ was converted into a multilocular cyst owing to stenosis of the upper end of the ureter. The infant was the subject of several other congenital malformations. The other kidney was normal.

The simplest form of change which affects the pelvis of the kidney is dilatation. This dilatation may affect the ureter, or it may not, and the question will be decided by the situation of the obstruction upon which the dilatation depends. As a rule, the obstruction is a calculus at the renal orifice of the ureter or in the course of the tube, but it may be a cicatrix which the former passage of a calculus has occasioned. The dilatation frequently proceeds until the whole kidney is converted into an irregular cyst, which is then known as a **hydronephrosis.**

Hydronephrosis may be congenital or acquired. In the former instance it is common, though not invariable, for both kidneys to be affected. The cyst which is formed varies in appearance and in size. As a rule, it has a somewhat irregular outline, and its walls are thin. It is lined internally by a single layer of flattened epithelium, and contains a watery fluid which somewhat resembles urine in its composition. In cases of congenital hydronephrosis the cyst is often multilocular.

Simple hydronephrosis is not a very common condition. This is intelligible when we consider that the principal cause is the presence of a calculus, and that such an irritant is very likely to lead to the formation of pus, and therefore to the production of a pyonephrosis.

When the ureter is affected under these conditions, it may be found to be dilated throughout its entire course, in which case the walls may be greatly thinned, but are more commonly hypertrophied, or it may be dilated close up to the pelvis of the kidney and contracted below. The latter state is particularly likely to be found if the hydronephrosis has resulted from the formation of a cicatrix in the ureter after the passage of a renal calculus. The ureter is then frequently found to be greatly elongated, and it may show definite kinks and twists, or it may be impervious in some portions of its course.

Calculous pyelitis is the usual condition met with when the pelvis of the kidney contains a stone. As a result of the irritation of the calculus the inflammation is accompanied by the formation of a large amount of pus, by the dilatation of the pelvis, and by its filling up with a large quantity of granulation tissue and dense cicatricial tissue. The affected kidney is enlarged, and when a section is made into it the great amount of yellowish-white material which fills the pelvis often leads to the supposition that a new-growth is present. In the midst of this mass of inflammatory material the calculus is found. As might be expected, the densest fibrous tissue is present at the furthest distance from the calculus, while immediately around it lies a delicate granulation tissue which is full of leucocytes ready to break down into pus. In cases of this description the ureter is not generally affected to a very considerable extent, though it suffers from the fact that it has to convey to the bladder the inflammatory material formed in the kidney. Its walls are thickened, and a certain amount of pus is formed by its inflamed lining membrane, but it is usually not highly dilated.

The commonest condition in which a suppurative pyelitis and ureteritis obtains is that in which an inflammatory condition originating in the bladder or below extends upwards. As a result of the obstruction to the flow of urine into the bladder, the urine collects behind the obstruction and dilates the ureters and pelves of the kidneys with the final production of surgical kidney. In the process the ureters are frequently dilated until they have a thickness of the forefinger or even more, their walls are thickened, and their lining membrane produces a considerable amount of mucus and pus. The same condition obtains in the case of the renal pelvis.

When the kidney is the seat of local tuberculous disease, the pelvis and the ureters always share in the affection. They are then thickened, and their lining membrane is converted into a layer of thick curdy material which is nothing more than caseous tuberculous material. A ureter thickened in this manner may easily be the size of the forefinger.

Before leaving the pathological anatomy of the ureters, it may be mentioned that sometimes one finds them, or one of them, blocked by a blood clot. This clot has been formed by the coagulation of blood that has escaped from the kidney itself. The matter is not important from a pathological point of view, but clinically it is important in that the symptoms to which the passage of the coagulum gives rise are identical with those which accompany the passage of a renal calculus.

(3) THE URINARY BLADDER

By far the larger number of pathological conditions which affect the urinary bladder are secondary, and, owing to the length of the male urethra and the diseases to which it is liable, and the existence of the prostate, disease of the bladder is commoner in males than in females.

(1) **Hypertrophy. Atrophy and dilatation.**—Under a number of conditions into which it is not necessary to enter, but essentially as the result of an obstruction of greater or less severity, the urinary bladder is liable to undergo alterations in the thickness of its walls. The laws under which hypertrophy or atrophy supervenes are those which determine the same factors in the case of all muscular tissue, and the actual appearances that obtain in the case of the urinary bladder are very like those which obtain under similar circumstances in the case of the heart.

When the walls of the bladder are hypertrophied the viscus is almost always contracted, and the muscular bands pass around and across the internal surface beneath the mucous membrane in so strongly marked a fashion that they recall the columnæ carneæ of the heart. This condition of the bladder is known as **fasciculation**, and it is only present in the case of a bladder which has become hypertrophied as the result of the presence of some obstruction that has existed for a considerable time. (Fig. 143.)

When the bladder is atrophied it is always dilated also, and then the wall may be no thicker than a sheet of paper. When the atrophy has occurred within a short time, and particularly when it has occurred in the absence of any definite obstruction to the outflow of urine, the wall is of even thickness throughout. But when, as is not uncommonly the case, the atrophy supervenes upon an hypertrophy with fasciculation, the thinning is most marked between the muscular bundles. As a result the fasciculation becomes more pronounced and a number of pockets, of which the walls are very thin, appear, and almost convert the bladder into a multilocular cyst, owing to the great superiority of their diameters over the diameters of their orifices.

Conditions such as the above may be simple, but far more commonly they are accompanied by other changes of which inflammation of the bladder (cystitis) is the chief. The cystitis may be the primary condition upon which the vesical changes depend, but it, too, may be secondary to some other condition.

(2) **Inflammation (cystitis).**—In cystitis the bladder is almost always contracted, and its walls are therefore thicker than normal, whether this be the result of hypertrophy or merely due to the fact that the muscular tissue of the wall is contracted. The mucous membrane is deeply congested and the congestion is most marked on the summits of the ridges into which the mucous membrane is thrown. The mucous membrane is itself thickened and softer than normal, as the result of its infiltration with inflammatory products, and it is always largely covered with a layer of tenacious mucus.

Microscopically, the bladder wall in cystitis shows the presence of an intense inflammation. The epithelium is in places desquamated, and in places it is heaped up as the result of a definite proliferation. The muscular wall itself shows the presence of great numbers of leucocytes in the intermuscular connective tissue, and the blood-vessels may be found full of blood. Hæmorrhages into the submucous tissue are not uncommon.

In cases in which the reaction of the urine has undergone a change from acid to alkaline, and in addition has become ammoniacal owing to the decomposition of the urea into ammonium carbonate as the result of bacterial action, there occurs a deposition of the phosphates of the urine within the bladder. These phosphates are a combination of the phosphates of calcium, magnesium, and ammonium, and they form a white amorphous material somewhat like plaster of Paris (except in its friability), which is deposited more or less thickly on the inflamed surface of the vesical mucous membrane.

The principal causes of cystitis are vesical calculus, enlargement of the prostate and stricture of the urethra, and in the female, uterine fibroids ; but any inflammatory condition obtaining in connection with parts in the neighbourhood of the bladder may extend to it and set up a local inflammation.

A special form of vesical inflammation is that which depends upon **tuberculosis**. Tuberculous disease of the bladder is always secondary either to tuberculosis of the kidney or to tuberculosis of the testis. It does not call for any special remark, beyond that it is associated with marked ulceration. At first the ulcers are small, have a depressed greyish base which shows the presence of caseous material, and are surrounded by heaped-up overhanging edges. Their appearance, in fact, is very similar to that of a tuberculous ulcer of the intestine.

(3) **New-growths.**—The bladder is not greatly liable to new-growths, although it is sometimes involved by the extension of a new-growth from neighbouring parts, particularly the cervix uteri in women. Such extension forms one of the most distressing conditions, for the existence of a fistula between bladder and vagina leads to an incontinence of urine which cannot be cured and can hardly be relieved. In the male an extension to the bladder of a carcinoma of the rectum leads to the establishment of a recto-vesical fistula, and the presence of fæcal material in the bladder leads to a cystitis that renders this condition hardly less distressing than the corresponding condition in the female.

Of primary non-malignant growths of the bladder, the only one of importance is the **villous papilloma**. This growth is almost peculiar to the bladder, although a growth of somewhat similar appearance is met with in the larynx. It is generally situated at the base of the bladder and springs from the mucous membrane close to the orifices of the ureters. It is a definite papilloma, with long delicate processes that do not generally show a great degree of branching. These processes consist of a central strand of delicate connective tissue which carries a relatively enormous capillary or more than one. Externally the process is clothed by a single layer of large spindle or columnar cells or by several layers of stratified epithelium which are cast off with great readiness, so that it is difficult to obtain a specimen in which they are well preserved. Macroscopically, the growth resembles a mass of red seaweed, and when placed in water the branches float out in exactly the same manner. The growth is of importance in that the processes are very apt to be torn off during the contraction of the bladder with micturition, and therefore lead to one variety of hæmaturia.

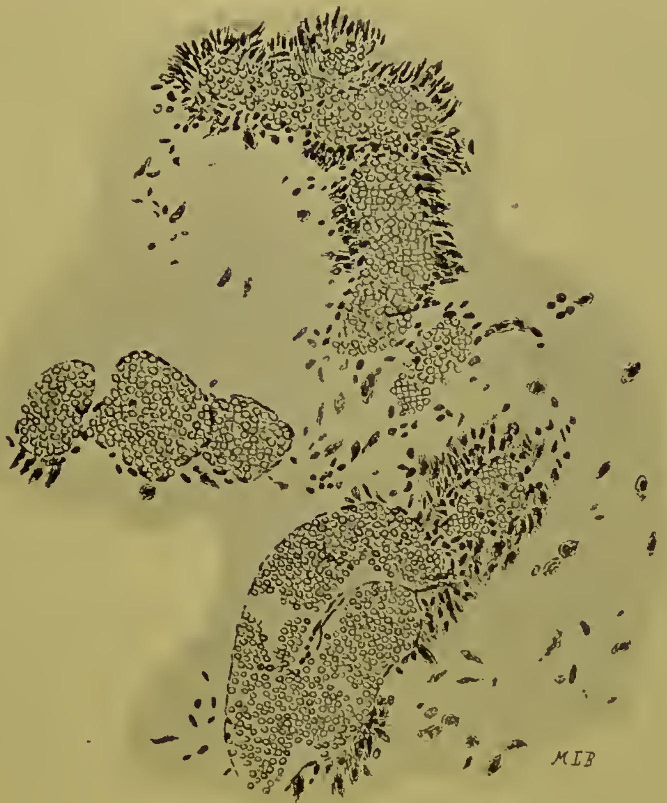


Fig. 134.—Portion of Villous Papilloma of Bladder passed in Urine. × 60.

Portions of several villi are seen. The growth consists practically of a very delicate connective-tissue framework, carrying large capillary blood-vessels, and covered by columnar epithelium. Isolated columnar cells are seen at various points of the figure.

Primary carcinoma also occurs in the bladder, but rarely. It forms a large mass, often having a 'cauliflower' appearance and being ulcerated. It is of the squamous-cell variety, and is often associated with the presence of a calculus.

(4) THE URETHRA

The most important pathological conditions of the urethra are **gonorrhœa** and its consequences. The disease itself is an intense specific catarrhal inflammation of the mucous membrane of the urethra, which generally at first affects only that portion which is close to the meatus, but which in females extends through the whole length of the tube, and in males extends as far back as the prostatic portion, in severe cases.

In the acute stage of gonorrhœa the mucous membrane of the urethra is intensely red and swollen. At first there is only a little secretion of a watery character. But in the course of a few days the character of the exudation changes until it becomes creamy and consists of pure pus. In this pus, the chief cells present are finely granular oxyphil cells, but a few coarsely granular oxyphil cells and hyaline cells are to be found. The finely granular oxyphil cells show the ordinary degenerative changes of the nuclei, in particular the nucleus is broken into three or four portions ; but they differ somewhat from ordinary pus cells in the great numbers of their granules and the brilliancy with which they stain with acid dyes. Unless a comparison be made between them and a cell which is a coarsely granular oxyphil cell beyond doubt, it is likely that the cells in gonorrhœal pus will be mistaken for the latter variety of oxyphil cell.

The specific micro-organisms of gonorrhœa will usually be found in large numbers in the pus. It is characteristic of this micro-organism that it is found lying within the cells in the great majority of cases. Occasionally one which is extra-cellular may be found. Not all the cells show the presence of gonococci, and when they are present in any cell, they are usually present in considerable numbers. In the case of extra-cellular gonococci it can be seen that the micro-organism is a diplococcus and that each pair of cocci is surrounded by a clear capsule. When the cocci are intra-cellular the diplococcal formation is clear, but it may be impossible to demonstrate the presence of the capsule. This may be because there is none, or, it may be because a number of diplococci are included in a clear space which lies within the cell, and which perhaps represents a vacuole formed in the process of phagocytosis, or perhaps a collection of capsules, of which the individual outlines of each are merged in the whole. (Plate IV.)

Microscopically, a section of a urethra which is the seat of gonorrhœa shows the presence of an intense catarrhal inflammation which extends deeply into the surrounding tissues and on the surface is accompanied by a considerable proliferation of the epithelial cells, with desquamation, and the admixture of a large number of pus cells. The papillæ of the corium are frequently elongated.

In a more advanced condition the process goes on to the formation of definite ulcers, and it is the cicatrisation of these which leads to the formation of **strictures** of the urethra. The contraction of the fibrous tissue of which a stricture is composed constitutes an obstacle to the outflow of the urine, and subsequently leads to those changes of the bladder, ureters, and kidneys which have already been described.

The only primary new-growth of the urethra, apart from those which are rather new-growths of the organs of generation, is **vascular caruncle**. This growth is of the nature of a papilloma, and is principally found encircling the orifice of the *female* urethra. Histologically, it consists of highly vascular connective tissue which is covered by stratified epithelium, and which, on section, shows that the epithelium lines clefts and pockets which dip into the deeper tissue. The epidermal lining for these pockets consists of the ordinary layers of the epidermis, but the effect of their section at right angles to their direction yields somewhat the appearance of an adenoma, while the cells themselves are similar to those which one meets in a rodent cancer. At the first glance sections of a vascular caruncle are apt to be puzzling.

(5) MALFORMATIONS OF THE URINARY APPARATUS

When we consider the complicated nature of the processes which go to build up the perfect urinary apparatus, it is not extraordinary that minor malformations of some part or other of the tract should be common. Perhaps the commonest of these is a persistence of fœtal lobulation. It is rarely great, but in a small degree is found with frequency. It is without pathological importance. Fairly common also are minor degrees of hypospadias—a condition in which there is a failure of the urethra to close on its under side. This condition is, however, far less common than a persistence of fœtal lobulation of the kidney.

More marked malformations consist in the formation of a so-called 'horseshoe kidney' from the union of the two kidneys at one or other extremity. The union is almost always at the lower extremity. In other respects the organs are generally normal; in particular there is usually no malformation of the ureters or the blood-vessels. This is, however, only true when the horseshoe condition is slight, as in the cases which one ordinarily meets. When the union is a considerable one, and especially when it concerns not one end of the organs, but affects the entire hilum on each side, the vessels and ureters are invariably abnormal in arrangement and probably also in number.

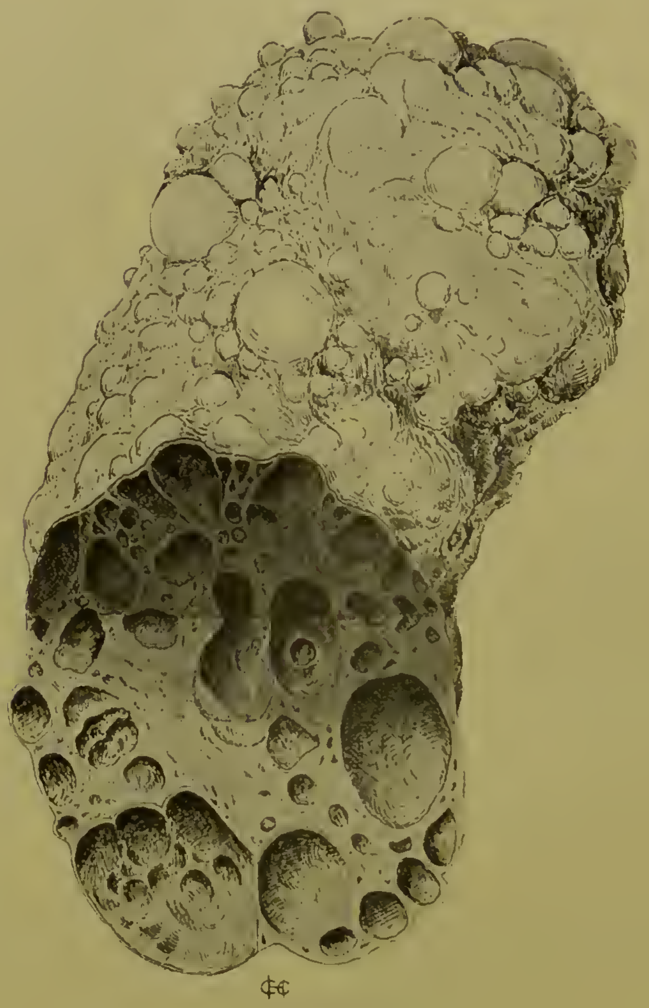


Fig. 135.—Congenital Cystic Disease of Kidney. $\times \frac{2}{3}$.

The organ is converted into a multitude of cysts of varying size, and little or no true renal substance is recognisable. A portion of the lower part of the organ has been removed to show that the condition is uniformly distributed.

To congenital hydronephrosis attention has already been directed, and it has been said that it is generally bilateral. Another condition of the kidney is known which is also (possibly) congenital, cystic, and bilateral, but which differs so considerably from hydronephrosis that it has received the name of **congenital cystic disease**. In this condition both organs are usually greatly enlarged, and there is often little but their position to indicate that they are altered kidneys at all. For the organs are converted into a number of cysts which vary in size from a pin's head to a walnut, and are filled with a watery or semi-gelatinous material that differs in colour in different cysts. There is frequently not the slightest trace of renal substance to be seen, and the effect of the cysts, with their different colours, suggests that of a mass of rounded uncut gems. It is not in all cases that the entire kidney is affected; sometimes a portion of the organ is apparently fairly normal.

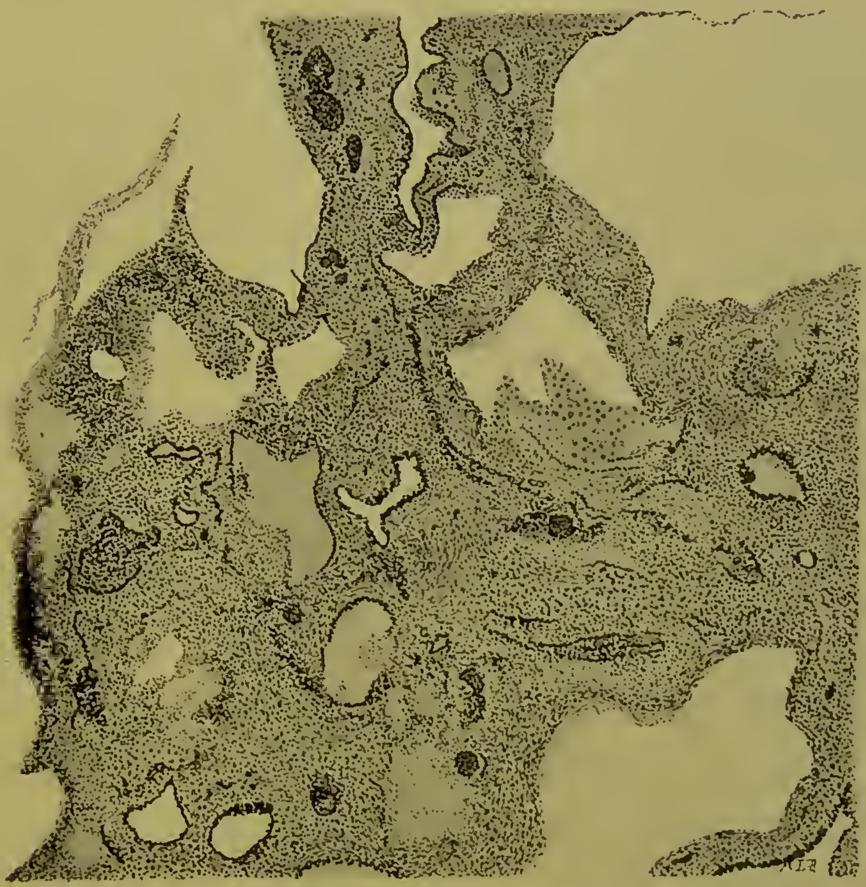


FIG. 136.—SECTION OF KIDNEY SHOWING CONGENITAL CYSTIC DISEASE. × 60.
The 'renal' character is completely lost, and instead there is a meshwork of fibrous tissue enclosing cysts of irregular size. The cysts are lined by a single layer of regular flattened epithelium, some of which (on the flat) is seen at the lower part of the cyst slightly to the right and above the centre of the figure.

In the case of the bladder the most important malformation is due to a failure in closure of the anterior abdominal wall, with the result that there is a deficiency of the front of the bladder. The mucous surface of the viscus is therefore exposed on the surface of the body, and the orifices of the ureters are to be seen at the lower part of the exposed and reddened surface. The condition is known as **extroversion** of the bladder. It is a somewhat rare condition and is always accompanied by some other malformation affecting, generally, the external organs of generation. Thus it is likely to be associated with an extreme degree of hypospadias. The malformation is not dangerous to life, so that individuals in whom it is present reach to adult age.

Malformations of the urethra always coincide with malformations of the external organs of generation. They are far more common in the male than in the female, and consist in a failure of the tube to close. This failure may occur on the under surface, which is far the more common, or on the upper surface. In the former instance the condition is termed **hypospadias**, in the latter **epispadias**. Epispadias is never very extensive, but hypospadias may affect the urethra through nearly its entire length.

(6) URINARY CALCULI AND ABNORMAL CONSTITUENTS OF THE URINE

Calculi are found both in the kidneys and in the urinary bladder, and the chief difference between them is that it is common for the vesical calculi to be covered by a layer of material which is wanting in the case of the renal calculus. This statement is not, however, of universal application, for sometimes the urinary changes which lead to the modification characteristic of the vesical calculus affect the urine as it lies in the pelvis of the kidney, and then no difference obtains in the character of the calculus as it lies in the kidney from what would have obtained if it had passed along the ureter, had reached the bladder, and had there set up the urinary changes.

Some forms of calculus are practically peculiar to the bladder, but the majority are common to both kidney and bladder, as might be expected. The only variety that is strictly peculiar to the bladder is that which consists solely of a combined phosphate of ammonium and magnesium. This forms a white crumbling calculus, but more commonly forms a coating for a calculus which has reached the bladder from the kidney, or is deposited upon any other foreign substance within the bladder or even upon the inflamed wall of the bladder itself. It occurs only when the urine is alkaline and ammoniacal. Other forms of vesical calculus are much rarer. The chief among them are calcium phosphate, calcium carbonate, cystin, and xanthin. Calculi composed of calcium phosphate and of calcium carbonate are hard, and generally white or dull grey in colour; cystin and xanthin stones are soft and coloured, cystin calculi being yellowish, but after exposure to air becoming of a turquoise-blue colour, and xanthin calculi being deep red. It is rare for any of the calculi that have last been mentioned to reach to any great size ; a calcium phosphate calculus may be as large as a walnut, but a cystin calculus is rarely larger than a large pea, and xanthin stones are considerably smaller. Both cystin and xanthin calculi are very rare.

In the majority of cases the central portion of a vesical calculus consists of a calculus which has been formed in the kidney. Renal calculi are chiefly of two kinds. The one kind consists of either pure uric acid or of urates of sodium and ammonium, or of a number of concentric rings of these different substances. Such calculi are hard; they may be single, but more commonly are multiple, have generally a fairly smooth surface, though they may be somewhat branched, and are generally of a pale fawn colour. The other variety consists of pure oxalate of calcium and forms a much-branched calculus of intense hardness and of a deep reddish-brown colour. It is generally single, does not usually reach to so great a size as the members of the other variety, and, from its appearance, has received the name of the 'mulberry' calculus. Of these two classes the former is by far the larger, and it can be further subdivided if it be recognised that in a great number of cases the character of a calculus is obscured until a section has been made through the middle. Thus, in spite of the fact that a calculus may appear to be composed entirely of phosphates, it is almost always the case that there is a central nucleus of some other substance—uric acid, for example. This nucleus may be so small that unless it is especially sought for it escapes notice. Even in the case of calculi that appear to consist solely of uric acid or some other single substance (e.g. cholesterin, in the case of a gallstone) a careful examination will generally show that there is a small central nucleus of organic material.

In the case of the urine the principal abnormal constituents that will come under our notice are the formed elements that exist in a deposit. Hence, albumin, which is in reality the commonest abnormal constituent of the urine, will not here call for any notice at all, except in so far as it enters into the composition of casts.

Blood when present in the urine is either found in the corpuscular form, or else the hæmoglobin is dissolved from the corpuscles, and though the urine may appear perfectly black from the amount of hæmoglobin which it contains, not a single blood corpuscle is to be seen. As a rule, when blood is present in the corpuscular form the fact is clearly recognisable with the microscope. The corpuscles themselves may be swollen, or they may be crenate, according to the composition of the urine, and particularly according to the amount of salts which it holds in solution. The spectroscope shows that it is rare for the hæmoglobin to be present in any other than the form of methæmoglobin. When the urine contains a large amount of blood that has been derived from the lower parts of the urinary tract, and particularly from the bladder or the urethra, the blood may coagulate and form definite clots. When the blood is derived from the kidney itself, excluding the pelvis of the organ, it never coagulates.

Pus in the urine is generally recognisable with ease, especially when it is present in any quantity. The urine is turbid on passing, and deposits a larger or smaller layer of a creamy fluid which consists almost entirely of pus corpuscles having the ordinary characters. A certain number of red corpuscles may also be present, but as a rule in a well-marked case they are very few. The principal conditions under which the urine contains pus are calculus of the kidney with pyelitis, vesical calculus, local tuberculosis of the kidney or of the bladder, and all the multitudinous conditions which are associated with cystitis. In the case of the latter disease the pus is mixed with a large amount of mucus which has been derived from the inflamed mucous surface of the bladder and perhaps also from the urethra.

A condition which may at first be mistaken for the presence of pus in the urine is that resulting from a varicosity of the lymphatic channels running in the submucous coat of the bladder. This condition (which depends upon the presence of one or other of the different varieties of filaria in the main lymphatic channels, and particularly in the thoracic duct) is associated with the presence in other situations of the creamy fluid normally found only in the lacteals of the intestine. As the result of their varicosity and the pressure to which they are exposed during action of the bladder, these lymphatic channels give way and discharge their milky fluid into the bladder. Chyle, therefore, comes to be mixed with the urine, and the condition of **chyluria** is established. It is generally easy to distinguish the two conditions even without recourse to the microscope, for the milky condition of the urine in chyluria bears a direct relation to the ingestion of food, and, in addition, the creamy deposit of a urine containing pus occupies exactly the opposite position with regard to the fluid itself to that occupied by the 'cream' of the chyluric urine. The latter, consisting of fat globules, of course rises to the surface when the urine is allowed to stand. In addition to the presence of a large number of fat globules, chyluric urine frequently contains a number of small round cells which are evidently lymphocytes.

Casts are solid formations derived from the urinary tubules which are frequently found in the tubules themselves in large quantities in the various inflammatory conditions of the kidney, but which may also be found in the urine. They vary considerably in size and in composition. So far as size is concerned, it is necessary to distinguish those which have been formed in the larger tubules, such as the convoluted, and those which have been formed in the narrower tubules, such as the ascending and descending tubules, the collecting tubules and the conducting tubules. The shapes, too, differ in the case of casts derived from these different sources. For casts which have been formed in the convoluted tubules are themselves twisted, whereas those which have been formed in straight and narrow tubules possess similar characteristics.

Since the composition of casts varies, a series of names has been adopted. In some cases the casts are obviously composed of desquamated epithelial cells. These form the 'epithelial casts;' they are generally found to have been formed in the convoluted tubules. Sometimes one finds that a cast is entirely composed of epithelial cells, but more commonly a few epithelial cells are present in a mass which constitutes a granular or a hyaline cast. Epithelial casts are found principally in cases of acute and subacute nephritis. From this character the attribute 'desquamative' has sometimes been applied to the forms of nephritis in question. 'Granular casts' appear to be formed by a disintegration of the epithelial cells in a former epithelial cast. They may be of either large or small size. 'Hyaline casts' are characterised by their ground-glass appearance, and are chiefly found in cases of nephritis of a chronic type. A variety of cast which is rarely seen but which may be confused with the hyaline cast is that in which the cylinder gives the reactions of lardaceous material. 'Blood casts,' of which the nature is immediately apparent by the colour, are common in forms of acute nephritis, whether active or receding. Occasionally a few small blood casts are found in cases of chronic renal fibrosis.

Bacteria are constantly found in urine that has been allowed to stand for a short time after passing, but this condition is entirely accidental. In cases of cystitis, however, the urine contains bacteria when passed, in a very large number of cases, and in certain instances the urine may be positively turbid from the numbers of bacteria that are present. This condition has been termed **bacilluria**, but bacilluria does not necessarily coexist with cystitis. Thus in a few cases of typhoid fever the passage of a turbid urine has been noted. That the urine in cases of typhoid fever contains the specific bacilli is certain, but a careful search is generally necessary to prove their presence. In the cases to which attention has just been directed, however, the urine constitutes what is practically a pure culture of the micro-organism. The conditions underlying bacilluria are not, as yet, understood.

Passing mention need only be made of the occasional presence in urine of **spermatozoa** and of the **ova of Bilharzia hæmatobia**. The significance of the presence of spermatozoa is unknown; their characters are generally unmistakeable, but it must be mentioned that care is necessary, when examining the urine of a female, not to confound them with certain of the animal parasites which are sometimes found to inhabit the vagina, and which may, therefore, gain access to the urine. The ova of Bilharzia hæmatobia are very characteristic. They are oval in form, and are provided with a spine at one end, or occasionally at one side; sometimes the embryo may be seen within them, and free embryos may be found at the same time in the urine. Their presence is associated with that of a large number of red blood corpuscles, since they are one of the most important causes of hæmaturia, particularly in Egypt and certain other tropical and subtropical regions.

Chemical deposits in the urine are of different kinds. By far the commonest is an amorphous material composed of the urates of sodium and ammonium. The substance is generally coloured to a greater or less extent by the uroërythrin of the urine, and constitutes the pink deposit that is so frequently observed when concentrated urine has been allowed to cool thoroughly. These urates are found only in highly acid urine. In alkaline or neutral urine one may also find an amorphous deposit which consists of calcium phosphate.

The crystalline deposits in urine are chiefly the following:

PLATE VII

Fig. A.—Crystals of margaric acid (above and to the left), of sodium biurate (above and to the right), and of cholesterin (below).

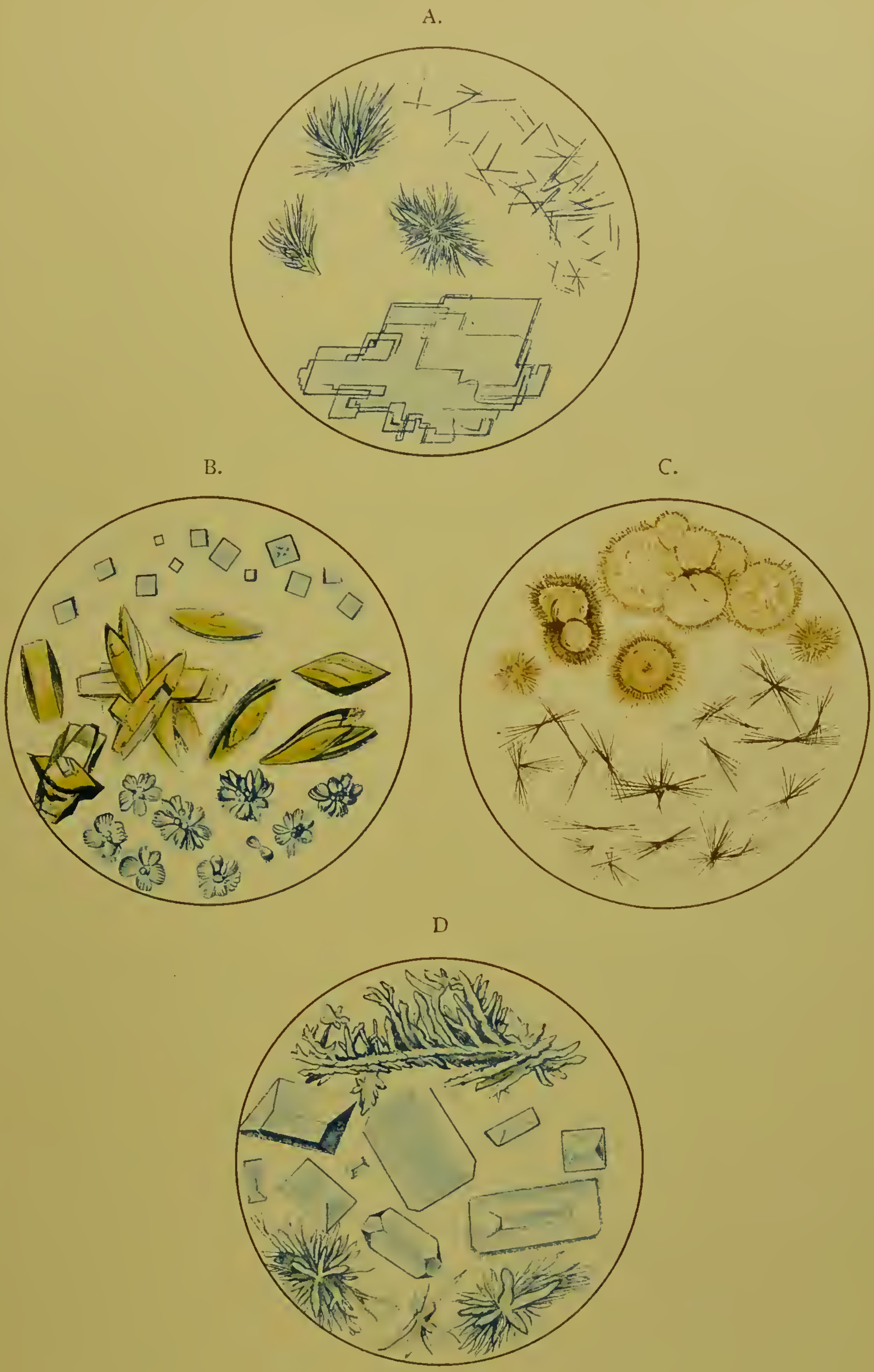
The magnification of the margaric acid and the sodium biurate is 420 diameters, of the cholesterin plates is 60 diameters.

Fig. B.—Crystals of oxalate of calcium (above), of uric acid (middle), and of acid ammonium urate (below). The uric acid crystals are magnified 60 diameters, the others 420 diameters. The crystals of acid ammonium urate ('hedgehog crystals') have been somewhat compressed to show that they are composed of sheaves of minute needles radiating from a centre. Apart from compression, they much resemble leucin (fig. C), but are far smaller.

Fig. C.—Leucin (above) and tyrosin (below). Magnification of leucin 60 diameters, of tyrosin 420 diameters.

Fig. D.—Ammonio-magnesium phosphate and crystalline calcium phosphate. All magnified 60 diameters. Above is seen the 'feathery' ammonio-magnesium phosphate, in the middle the common 'sarcophagus' form of the same substance, below are three bundles of calcium phosphate. The latter substance is here shown in the 'stellar' form ; usually calcium phosphate in urine is amorphous.

Plate VII.



Crystalline Deposits.

Uric acid, present in small grains resembling cayenne pepper, which microscopically are seen to be in the shape of whetstones or lozenges, and to have a yellow colour in the majority of cases. The crystals are often arranged in sheaves or bundles. Other crystalline forms are known to occur in urine, but the above-mentioned is the most common. The shape and colour are due to the fact that the crystals have formed in the urine. When they are chemically pure they are colourless and form rhombic rectangular plates or rectangular prisms.

Calcium oxalate, which forms small regular octahedra resembling envelopes. The crystals are colourless and vary but little in size. Occasionally calcium oxalate is found in the form of dumb-bell crystals.

Ammonio-magnesium (triple) phosphate.—This substance is found only in urine that has undergone the ammoniacal decomposition. It forms colourless crystals that vary considerably in size, but are generally far larger than any of the other varieties of urinary crystal. The shape is a triangular prism ('tombstone' or 'coffin-lid' crystals). When the crystals are small and have fairly equal sizes, they may resemble crystals of calcium oxalate somewhat closely. Occasionally the substance crystallises in a 'feathery' form.

Calcium phosphate, in addition to its commoner amorphous form, may crystallise in the form of rosettes of prisms ('stellar phosphates').

Leucin forms yellowish-brown spheres of large size which consist of masses of needle-shaped crystals. It is always found along with tyrosin, and hardly occurs except in cases of acute yellow atrophy of the liver and phosphorus poisoning.

Tyrosin crystallises in long slender needles which are generally arranged in groups or sheaves.

Cystin occurs in regular hexagonal plates. It is very rarely seen. The same is true of xanthin, which forms lemon-shaped crystals.

Acid ammonium urate is formed in alkaline urine, especially if it has stood for some time. It is deposited as spiked globular masses which consist of agglomerated needles arranged in sheaves ('hedgehog crystals'). The masses are of small size, and are not often found.

SECTION XV

THE ADRENAL BODIES

The adrenal bodies are subject to but few pathological changes, but one of them, viz. tuberculosis, is of great importance and not very uncommon.

Malformations of the adrenals are uncommon, if we except the presence of accessory adrenals and the existence of adrenal 'rests.' Accessory adrenals are very variable in size and number, and, although fairly common, are not so common as accessory splenules. They are of no pathological importance. Adrenal rests are important in that it is believed that they may be the seats of origin of new-growths. The chief situation in which the rests are found is the kidney, but they may be present as far away from the main bodies as the broad ligaments of the uterus.

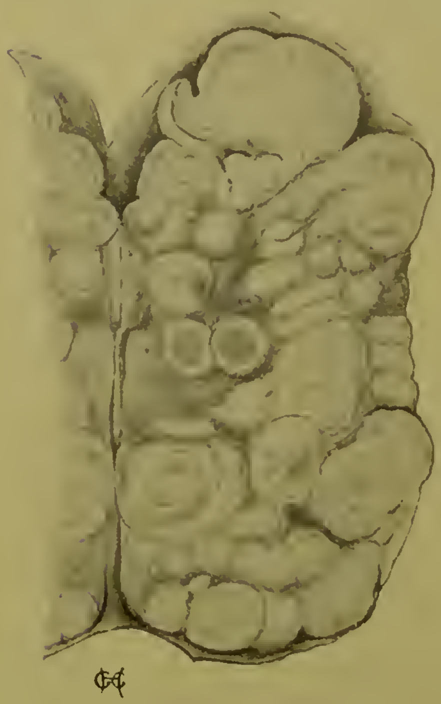


FIG. 137.—ADRENAL BODY FROM A CASE OF 'ADDISON'S DISEASE.' NATURAL SIZE.

The gland is enlarged and completely replaced by a number of foci of tubercle that have undergone caseation. As a rule the foci do not show central softening.

On rare occasions the adrenals are found to be the seat of **hæmorrhage**. When this occurs the blood is found to replace the greater part or the whole of the medullary portion. Little is known of the conditions under which hæmorrhage takes place in the organs, but it appears that the principal condition that underlies the change is a severe toxic infection.

Tuberculosis of the adrenals is accountable for the production of Addison's disease. The disease itself is characterised by the supervention of severe and increasing anæmia and weakness, with a tendency to spontaneous hæmorrhages, and a peculiar bronzing of the skin and certain mucous surfaces. The change in the adrenals consists in a caseation which may readily affect the entire organ on each side and may lead to a not inconsiderable increase in their size. Occasionally the caseous material undergoes softening, but more commonly this is not the case. The tuberculosis occurs in some cases as the result of an extension from vertebræ that are affected with tuberculosis, but in others the disease seems to be primary in the adrenals themselves.

The **new-growths** of the adrenals are almost always malignant and are generally sarcomata, but may be carcinomata. In the latter instance it is often found that the growth shows the presence of those large cells arranged in more or less parallel columns that are characteristic of the cortical portion of the adrenal body itself. This peculiarity also obtains in the case of the new-growths which arise in the kidneys and elsewhere and which are supposed to have originated in adrenal rests. In some cases malignant growths of the adrenals are associated with alterations in the skin, particularly consisting in a great growth of hair in the axillæ and over the pubes. When the malignant new-growths of the adrenals occur in young children, the change, associated, as it may be, with an enlargement of the external generative organs and a marked alteration in temperament, frequently gives to the disease a striking character.

SECTION XVI

THE MALE GENERATIVE ORGANS

In some degree the pathological changes affecting the male generative organs have been dealt with when we were considering the urinary organs, but there still remain a few conditions which are particularly associated with the generative system where it coincides with the urinary, i.e. the penis and prostate, and the entire list of those which affect those parts which are strictly concerned with generation, i.e. the testes and vesiculæ seminales.

(1) THE PENIS

Apart from gonorrhœa and malformations, which are considered elsewhere, the penis is the seat of various forms of inflammation and of new-growth.

Among the inflammations we have those which are dependent upon special causes such as syphilis, and others which depend, apparently, upon the ordinary pyogenetic micro-organisms, although the form of inflammation which is produced is somewhat special. In addition to these we have non-specific inflammations, which are generally localised to particular regions. One of the commonest forms of non-specific inflammation is that which constitutes balanitis (inflammation of the glans) and posthitis (inflammation of the mucous surface of the prepuce). It is due to a want of cleanliness and to an accumulation of smegma beneath the prepuce, but is frequently combined with the presence of gonorrhœa, or a preputial soft sore, or syphilitic chancre. Its occurrence is often associated with the presence of a tight prepuce which cannot be retracted over the glans (phimosis). It is, indeed, principally by reason of the accompanying phimosis that balanitis and posthitis are of importance, for the looseness of the preputial tissue is an important factor in aggravating the phimosis by reason of the large amount of inflammatory exudation which it will hold. Apart from phimosis, a little care is sufficient to cure the inflammation, but the congestion and accumulation of exudation fluid may be so great that it is not only quite impossible to retract the prepuce, or impossible to draw it forward again when once it has been retracted (paraphimosis), but even a gangrenous condition of the prepuce or the end of the penis may supervene.

A somewhat more special form of inflammation is that which constitutes the venereal '**soft sore**.' Here, again, we have an inflammation which does not depend upon a specific micro-organism, and yet the sores are infective and are always conveyed by direct infection. In this case also there is reason to believe that lack of personal cleanliness plays a large part in their initial appearance, although it need not necessarily share in their dissemination.

A variety of ulcerative inflammation which is seen in the case of the generative organs is that which is termed **phagedæna**. In phagedæna we have an intense inflammation which runs a very rapid and destructive course. In fact, it is a variety of spreading gangrene, and as such is in no wise specific. Nevertheless the generative organs constitute a part in which such inflammation is particularly likely to occur. For not only are the tissues very loose, so that once an inflammation has commenced to spread, its course is liable to be very rapid, but also the starting point of a phagedænic ulceration is probably a soft sore or a gonorrhœa which has led to ulcerative balanitis. An important factor in favouring the occurrence of phagedæna is a poor constitutional resistance on the part of the patient, so that the condition is especially seen in the case of the very lowest classes. Phagedæna is less commonly met with at the present day than it was formerly, and of this more than one explanation is possible. The most probable explanation is that at the present time soft sores are recognised as being non-syphilitic, and therefore patients who exhibit them are not treated with mercury. Moreover it is not customary to give the large doses of mercury in the treatment of syphilis that were formerly thought to be necessary. Its disappearance must probably be directly associated with a discontinuance of the practice of mercurialisation.

Of the new-growths affecting the penis, one, the **papilloma** or **wart**, is distinctly associated with inflammation. The warts themselves generally spring from the furrow behind the corona, but they may also grow from the inner surface of the prepuce and the glans. They may form a mass so large that it conceals the entire end of the penis.

Microscopically, the growths are ordinary papillomata, but owing to the large amount of moisture which is present in their neighbourhood the layers of epithelial cells which cover them are apt to be very numerous. Centrally there is a small quantity of fibrous tissue which carries small nutrient blood-vessels.

Although papillomata on the penis are so frequently associated with gonorrhœa that they are sometimes termed gonorrhœal warts, other forms of irritation may lead to their appearance. Of these the most important are dirt, and retained secretions or discharges; they may also occur in association with syphilis, and then they are closely allied to the condylomata.

Malignant disease of the penis is almost always of the epithelial type, although a few cases of sarcoma have been described. The new-growth may show itself as a wart with ulcerated surface and hard edges, or it may appear as a definite ulcer. It generally begins in the sulcus behind the glans, and spreads thence to neighbouring parts, ultimately involving the skin of the penis. In an advanced case it may appear either as a deeply excavated ulcer or as a cauliflower growth which discharges a foul sanious fluid. The condition is very liable to be associated with a long-continued irritation such as that which depends upon phimosis. Under these circumstances the carcinomatous ulcer may form beneath the prepuce and not be recognised until it has ulcerated through the skin and has formed a fungating mass.

Microscopically, the growth is a squamous-cell carcinoma, but it differs somewhat from the ordinary in the facts that there is rarely so large a degree of down-growth of epithelium into the deeper tissues, and that cell nests are somewhat uncommon. Hence the growth approximates very closely, so far as its microscopic appearances are concerned, to the ordinary papilloma. As we shall see later, carcinoma of the cervix also tends to separate itself somewhat from the other varieties of squamous-cell carcinoma in the same respects.

Affections of the skin of the penis we shall mention along with affections of the scrotum.

(2) THE TESTES AND THEIR COVERINGS

Inflammation of the testis (**orchitis**) is practically never seen as a primary condition, but always in association with or as a sequel of some other affection. The commonest of these is gonorrhœa so far as the acute inflammations are concerned, but among the chronic inflammations we meet with pathological changes in the testis dependent upon tuberculosis and syphilis. It may also arise from direct injury or supervene in the course of certain of the acute infective fevers of which **mumps** is the commonest.

The condition is intensely painful and the part is somewhat swollen. As a rule the inflammation does not go on to suppuration, but the latter change may occur. Even in the non-suppurating orchitis the inflammation extends to the scrotum, which becomes red, swollen, and glistening from the large amount of inflammatory exudation in the cellular tissue, and when suppuration occurs the scrotum definitely becomes involved in the process of pointing of the abscess. The final result of suppuration is generally a complete destruction of the testicle, but hernia testis may occur.

Epididymitis is almost always caused by the extension of an inflammation affecting the membranous or the prostatic portion of the urethra, and consequently its chief cause is gonorrhœa. The appearances are similar to those which are found in orchitis, except that the fact that it is the epididymis that is affected is shown by the localised swelling at the back of the testis. The condition may pass into a chronic form or it may end in suppuration. It may occur in conjunction with orchitis or independently.

Tuberculous disease.—Tuberculous disease of the testicle may be a portion of a general disease of the genito-urinary tract, or it may be localised to the testicle, or tuberculosis may be present in other parts of the body than the testicle and genito-urinary tract—for example, in the lungs.

Tuberculosis of the testicle always affects the epididymis first, and in a large number of cases the body of the testis remains unaffected even to the last. Sometimes, however, it is found that the body of the testis has become affected, and then one finds small caseous foci in the body that are generally of a fairly uniform size, and are arranged in lines stretching from the posterior surface of the organ into its substance along the lines of the seminal tubes. The tuberculous foci always show a marked degree of caseation, and as a rule the caseous material is soft and ready to break down into curdy pus. A considerable amount of fibrous tissue is frequently formed in the neighbourhood of the foci. So much is this the case that the microscopic appearances are usually those of a dense scar tissue with associated caseous material in the neighbourhood. In such cases there is nothing that can indicate the tuberculous nature of the disease, so far as the microscope is concerned, but in other cases we may meet with typical tubercles, and may be able to find the specific bacillus, though this is far more difficult.

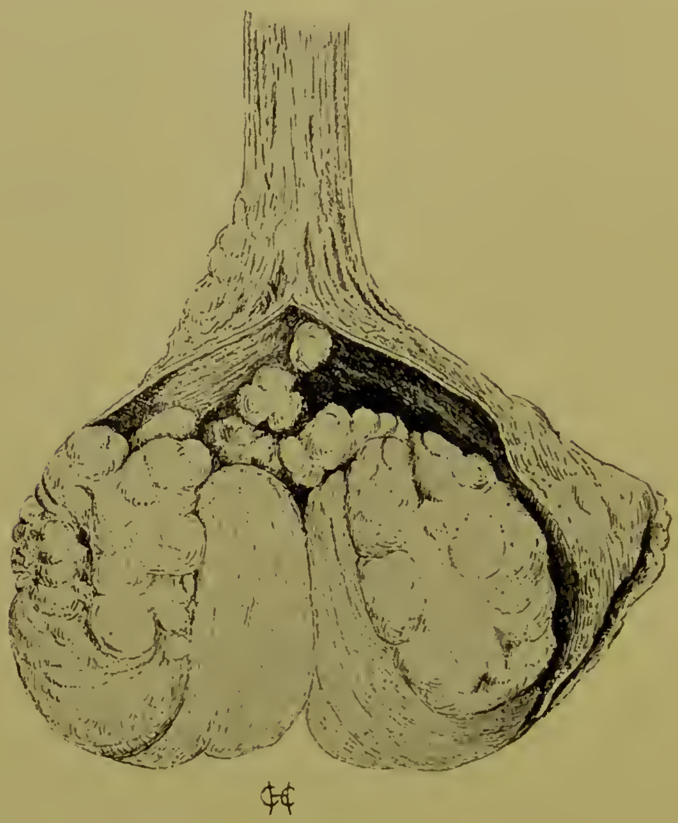


FIG. 138.—TUBERCULOUS TESTIS (OPENED FROM BEHIND). × $\frac{5}{6}$.
The epididymis is converted into a caseous mass, and similar caseous masses extend up the spermatic cord, which is much thickened. The body of the testis is practically normal.

As the disease extends the various parts of the epididymis become merged into one thickened and caseous mass which tends to soften at one or more points and to involve the skin. When this occurs the skin gives way and a sinus is formed through which the tuberculous material discharges itself, and through which a portion of the testis may protrude. Such a 'hernia testis' is far more commonly associated with and dependent upon tuberculous disease than upon any other cause.

The disease also extends up the cord, first of all manifesting itself by a uniform thickening, and subsequently by the formation of caseous foci along the course of the cord itself. These foci are generally somewhat isolated from one another at first, but later they become continuous. From this point the disease proceeds to involve the vesiculæ, the prostate, and probably the bladder.

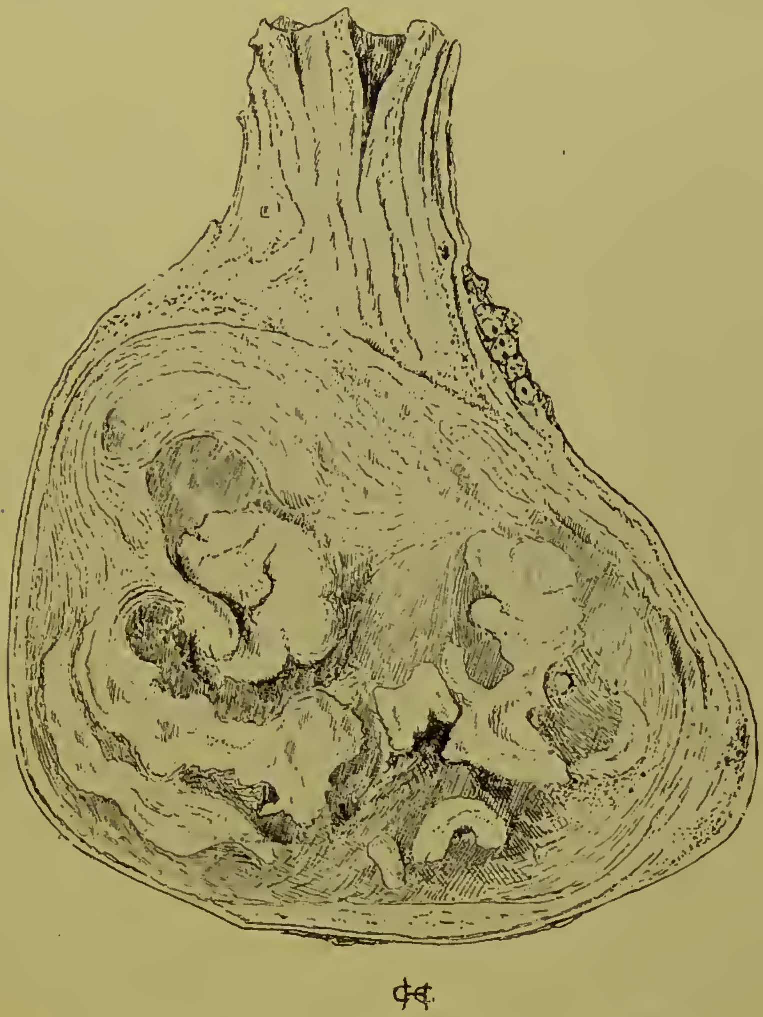


Fig. 139.—Gummata of Testis. Natural Size.

The body of the testis is enlarged, and is replaced by a mass of firm fibrous tissue, in the centre of which are numerous foci of caseation. The spermatic cord is thickened and very firm.

Syphilis.—Syphilis shows itself in the case of the testis in two distinct forms. In the one there occurs a fibrosis which affects the body of the organ, and in the other gummata are formed.

In the syphilitic fibrotic testis the organ is generally somewhat diminished in size and of great hardness. The fibrous tissue is present chiefly in the body of the organ and is irregularly disposed. It appears to originate in connection with the intertubular connective tissue of the organ, but when the disease is pronounced the fibrous tissue is found in irregular masses, which replace small tracts of testicular substance. The epididymis also shares in the change to some extent, and the spermatic cord is likely to be denser than normal, but these changes are relatively small compared with the great alteration of the testis itself.

When syphilis attacks the testicle in the form of gummata, it is also the body of the organ that is affected. The testis is enlarged, unless the gumma is of very small size, and it may be the size of a Tangerine orange. It is firmer than normal, and, on section, it is seen that the body of the testis is replaced by a mass of tissue which consists partly of caseous material, and partly of newly formed fibrous tissue. The caseous material is collected into foci, and it does not seem to have the same tendency to undergo softening that is characteristic of the tuberculous caseous material when the epididymis is affected. The epididymis in syphilitic disease is generally fairly free, except for a share in the fibrosis which is present. This participation in the fibrosis may, however, cause the epididymis to become merged in a general mass of fibrous tissue by which the entire organ is surrounded.

Fibrosis. — Apart from the fibrotic conditions which have hitherto been mentioned, the testis is liable to be the seat of a fibrosis under two other sets of circumstances. A certain small degree of fibrosis accompanies the atrophy which occurs in old age. It is not, however, great, and consequently the senile testis is of a soft consistency. At the same time the organ diminishes considerably in size. A fibrosis also occurs constantly in testes which have failed to descend into the scrotum. Such 'retained testicles' are smaller than normal and usually very soft. Nevertheless they are the seat of a pronounced fibrosis along with a corresponding deficiency of testicular substance. The same is true of testicles that have descended, but have failed to undergo development at puberty. The actual degree to which the testis is altered in cases of retained testis varies considerably. In some cases the organ is but little changed, but in others it is more by its position and general shape that its testicular nature is discoverable. While dealing with this subject, it may be mentioned that a retained testis is sometimes the seat of an intensely acute inflammation. It then becomes greatly congested and swollen, and actual extravasation of blood may take place into the tunics.

New-growths.—Testicular new-growths are almost always of malignant nature, and are far more commonly sarcomatous than carcinomatous. So far as the growths themselves are concerned, it is usual for the general globular shape of the organ to be maintained, although there is a great increase in size. Thus a sarcoma of the testis may be as large as an infant's head. The growths are very frequently hæmorrhagic to a great degree, so that, on making a section of a tumour, it appears as if the central portion consisted of nothing more than blood clot. The same hæmorrhagic character is also noticeable in the secondary growths.

Microscopically, testicular growths are generally of the round-cell sarcoma type, but carcinomata are known. It is impossible to state in general terms what is the type of carcinoma present, excepting that it is never of the squamous-cell variety. As a rule, it is even difficult to decide as to whether the growth is sarcomatous or carcinomatous, especially as examples are known of carcinomata of the testis into the composition of which there enters a certain amount of hyaline cartilage. Such a combination is unknown in any other part of the body except as an accident.

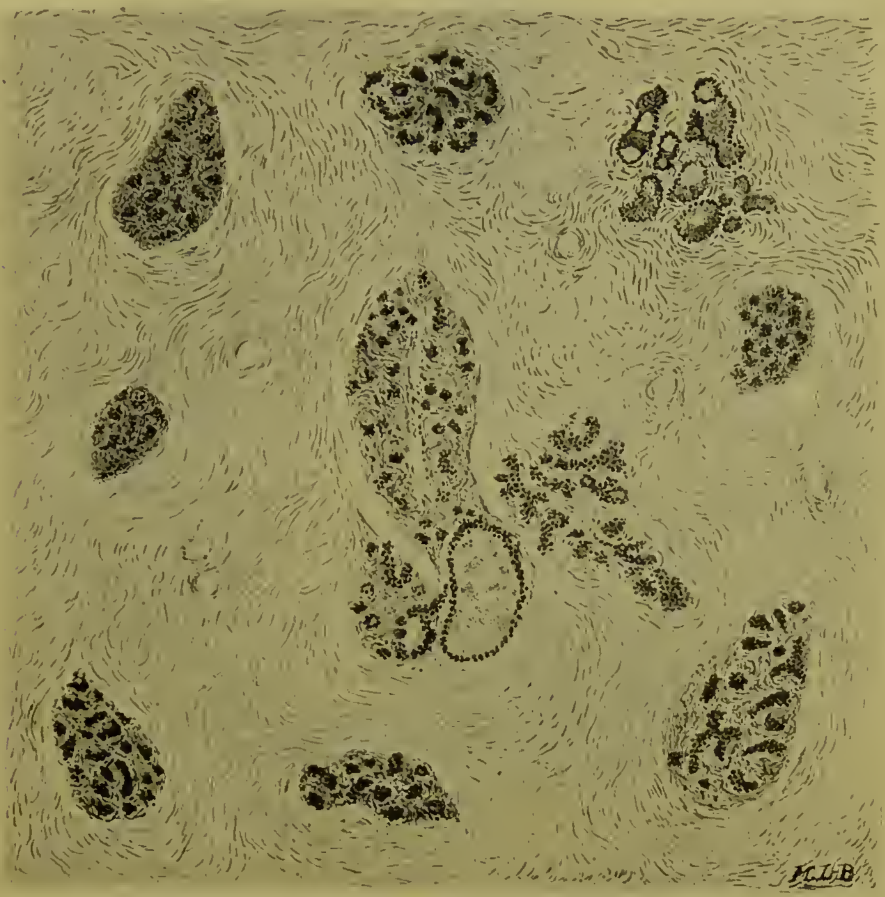


Fig. 140.—Section of Retained Testicle. × 60.

The organ consists of fibrous tissue from which nuclei are almost completely absent, and in which irregular foci of abnormal seminal tubules are visible. The lumina of the tubules are barely recognisable.

In a large number of cases testicular growths are cystic. In some cases these cysts appear to be the result of degenerative processes, and this is particularly the case when the contents of the cysts are colloid material, but in other cases the growth is of the cystic adenomatous type from the first.

The composition of the cystadenomata of the testis is very complicated. They may consist of cartilage or of fibrous tissue, but more commonly the solid substance consists of a mixture of fibrous tissue, myxomatous tissue, cartilage, and a varying amount of cartilage and perhaps strands of striated muscle. In addition, the lining of the cysts may be a simple or a compound epithelium. it may be ciliated or non-ciliated, and in not a few cases it vividly recalls the appearances of the ordinary epidermis. Under these conditions it is best to term the tumour a teratoma. In some cases there is an intracystic formation of papillary growths, and then the tumour has close resemblances to the villous columnar-cell carcinoma (papillary cystadenoma) of the kidney and ovary.

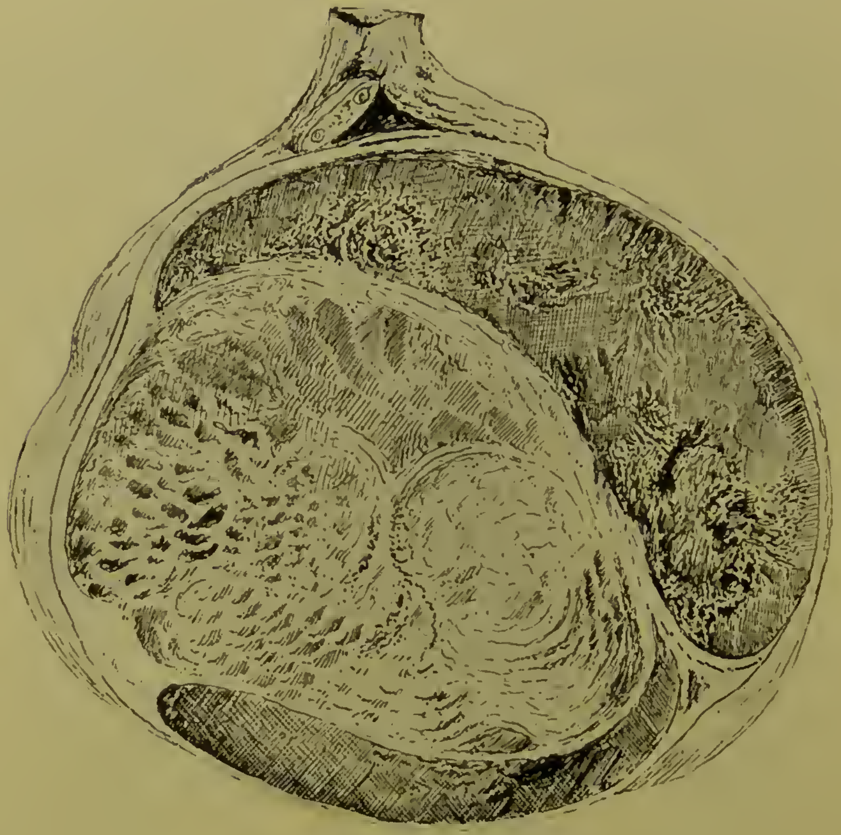


Fig. 141.—Hæmorrhagic Sarcoma of Testis. Natural Size.

The organ is replaced by a mass of sarcoma which in the periphery has been the seat of much hæmorrhage. Great enlargement has taken place in the testis, but the spermatic cord is fairly normal in this instance.

Dermoid cysts of the testis are occasionally met with, but are very rare.

The tunica vaginalis is apt to be involved in any morbid condition which affects the testis itself, but it may be affected independently. The principal condition under which this occurs is that in which an accumulation of fluid takes place within the vaginal sac. In the majority of cases this fluid is serous, and the collection of fluid constitutes a **hydrocele**. Sometimes, however, and particularly after a hydrocele has been tapped, the fluid within the vaginal sac is blood, and then the condition is known as **hæmatocele**.

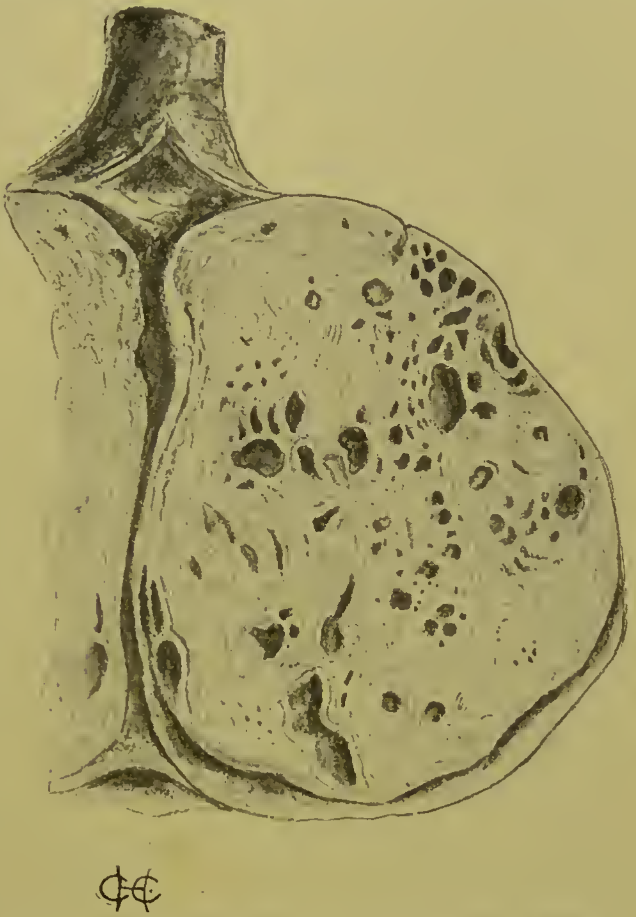


Fig. 142.—Fibrocystic Disease of the Testis. Natural Size.

The organ is enlarged, is of cartilaginous hardness, and shows numerous cysts. The solid portions in this instance showed great diversity of structure, but parts were apparently sarcomatous.

Hydroceles are of two distinct kinds, vaginal and encysted. A vaginal hydrocele is such as has just been described. The collection of fluid lies in front of the testis, and, owing to the nature of its contents and its coverings, is translucent. It may be quite small or it may be as large as a cocoa-nut. Its wall is generally fairly thin, but after repeated tappings the wall becomes greatly thickened. An encysted hydrocele, or a hydrocele of the cord, is always much smaller than the majority of vaginal hydroceles. It differs, too, in the fact that it is attached to the spermatic cord and not to the testicle. Its contents are milky in appearance, and spermatozoa are likely to be present in the fluid.

The spermatic cord is chiefly affected by pathological conditions, which have extended to it from other parts and particularly from the testis. To most of these reference has been made in passing. Of conditions which are peculiar to the cord itself, the most important is **varicocele**, which consists in the existence of a varicose condition of the spermatic veins. The dilated and tortuous veins are easily to be felt through the integument, and convey a sensation that has been likened to a bag of worms. So far as the pathological condition itself is concerned, there is nothing to call for special remark; the veins are altered in the same way as varicose veins in other situations.

Vesiculæ seminales.—These parts are generally affected only as the result of an extension of some disease which has attacked the vasa deferentia. Hence the principal change to which they are liable is a participation in tuberculosis of the testis, which has extended far upwards. Catarrh of the cavities, however, sometimes occurs, and the presence in them of concretions has been from time to time described.

(3) THE SCROTUM

Apart from that involvement of the scrotum in a tuberculous or a gummatous condition of the testis, or in orchitis, whether suppurative or not, to which attention has been directed in connection with the particular testicular diseases, the scrotum shows certain well-marked changes which are dependent partly upon the situation of the part and partly upon the character of the skin of which it is composed.

Œdema.—Under all conditions in which the skin is apt to become œdematous from other than definitely local causes, the scrotum is liable to show the accumulation of fluid to the greatest extent. This is very noticeable in cardiac failure and acute renal disease. In such cases the scrotum and the skin covering the penis are often converted into large bladders which have a translucent appearance from the amount of fluid which they contain within their meshes. In this way the scrotum may become as large as a small melon.

Another condition which is often very manifest in the case of the scrotum and the penis is **elephantiasis**. In this condition there is an interference with the passage of the lymph along the lymphatics, with the result that they become dilated and tortuous and induce nutritive changes in the skin itself. The characteristic alteration is a great thickening of the skin, with a roughness and irregularity of the surface. The actual amount of enlargement is sometimes so considerable that the scrotum hangs between the thighs as a tumour which weighs, perhaps, eighty pounds, and that the penis is lost in the general overgrowth of the scrotal and penile skin. The only evidence of its existence is a minute opening, which is probably indiscernible until it is seen that it is the spot from which the flow of urine takes place. With regard to elephantiasis itself as a disease we shall not concern ourselves here. It will be considered along with other morbid conditions of the skin.

The two most important diseases of the scrotum which are dependent principally upon its position are **eczema** and **carcinoma.** Eczema calls for no especial notice here. Carcinoma forms an irregular ulcer with hard everted edges which spreads locally and invades the lymphatic glands of the groin. Histologically it is a squamous-cell carcinoma.

(4) THE PROSTATE

By far the most important pathological change of the prostate consists in its *enlargement.* This is apt to take place in men over fifty years of age, and is accountable for the great majority of bladder troubles occurring in such persons. The enlargement may be uniform, or it may affect portions of the gland. Thus there may be a localised enlargement of the middle lobe, and this is the commonest condition, or the lateral lobes may be affected. The enlargement is often considerable. Where it is uniform the organ may be as large as a cocoa-nut, and an enlarged middle lobe may be the size of an orange. When the lateral lobes are enlarged, it may not be possible to determine the fact on opening the bladder from above, but when the middle lobe is enlarged it projects into the vesical cavity and is very obvious. Under any circumstances an enlargement of the organ causes interference with the passage of urine, but when the lateral lobes are increased in size, the effect is a constriction of the prostatic urethra; whereas, when the enlargement concerns the middle lobe, the obstruction consists in the fact that the enlarged lobe acts as a valve, and, in attempts at micturition, closes over the vesical orifice of the urethra.

An enlarged prostate may show, microscopically, several different conditions. The commonest is that in which the appearances are very similar to those of an ordinary fibro-adenoma, with the additions that the clefts and cysts may show the presence of corpora amylacea, and that the intercystic stroma contains a greater or smaller amount of unstriped muscle (fig. 38). In other cases the overgrowth may be due to a condition which is but little different from an ordinary leiomyoma, such as one meets with frequently in the uterus, or fibrous tissue may constitute the bulk of the enlargement, though this is far less common.

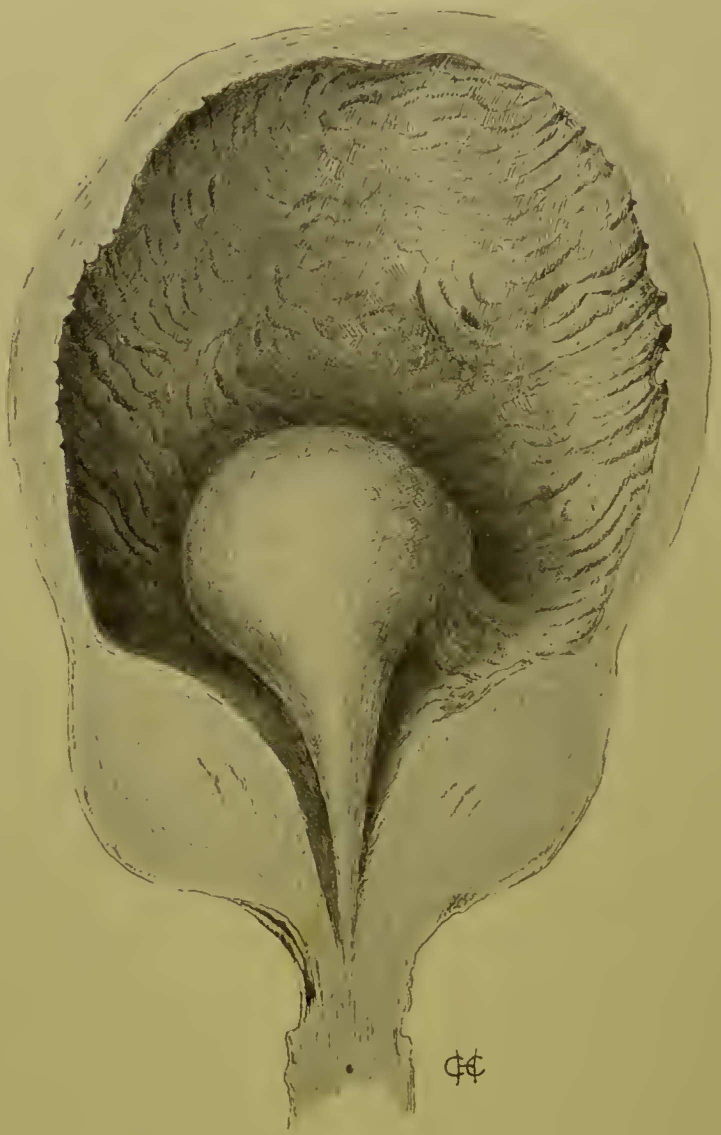


Fig. 143.—Prostatic Enlargement with Vesical Changes. × $\frac{2}{3}$.

There is enlargement of all the lobes of the prostate, but the middle lobe is involved to the greatest extent and projects into the cavity of the bladder. The wall of the bladder is greatly hypertrophied and fasciculated.

In rare instances the prostate is the seat of a malignant new-growth. As a rule this is a spheroidal-cell carcinoma of an intensely scirrhoid type which does not lead to any great enlargement of the organ.

The prostate is also liable to participate in diseases which have originated elsewhere and have spread to it. Thus we may have inflammation which sometimes goes on to suppuration and the formation of an abscess. Such a condition will probably depend upon an extension of gonorrhœa from the urethra or of a septic cystitis, or of any similar condition affecting the pelvic parts. So, too, tuberculosis of the prostate is probably never a primary condition, but results from an extension of the disease either by way of the vasa deferentia and the bladder, or by way of the ureters and the bladder.

The ducts and acini of the gland are sometimes the seat of **concretions**. Some of these are quite small, so that they are only visible with the microscope, others are larger (but rarely greater than a hemp seed), and are of a deep brown or black colour, while yet others reach to a considerable size. The smaller concretions often show a concentric arrangement on section similar to that found in grains of starch; they also give the same iodine reaction as lardaceous material. These constitute the 'corpora amylacea.' The large varieties constitute definite calculi and consist principally of carbonate of lime.

Cowper's glands are not of great importance from a pathological point of view, but they may become affected in the course of a urethral inflammation, and may suppurate, or, in children, their ducts may become obstructed, so that retention cysts are formed which project into the membranous portion of the urethra and may interfere with the passage of urine.

SECTION XVII

THE FEMALE GENERATIVE ORGANS

(1) THE VULVA

The labia are affected with **œdema** to a great extent in those diseases in which dropsy is a marked symptom, and from the looseness of the tissue of which the labia consist the amount of distension by the œdema fluid is as considerable as in the case of the scrotum. So, too, when the vulva is the seat of **elephantiasis** the enlargement of the labia is a very prominent feature. They often form tumours weighing several pounds, and may hang down as far as the knees. The occurrence of **warts** in the neighbourhood of the vulva is even more common than about the glans penis, and gonorrhœal infection is also the commonest cause of their appearance. The vulva is also liable to an inflammatory condition (**vulvitis**) similar to that constituting balanitis and posthitis, which generally arises in ill-tended children and is associated with great œdema and redness of the parts, and with the production of a purulent discharge. **Carcinoma** affects the external generative organs in the female as in the male, and the growth produced is of the squamous-cell variety. It generally commences in one of the labia or in the immediate neighbourhood of the clitoris, and extends with the formation of deep ulcers having hard raised edges.

A formidable condition is that known as **noma**. It is a gangrene affecting the whole vulva or a portion of it, and is met with principally in ill-fed children, particularly when they have been attacked by some infective disease, such as measles or scarlatina. So far as appearances are concerned, they are similar to those which accompany noma of the face. The condition is very likely to end fatally after a considerable portion of the vulval tissue has become involved. A condition which is closely akin to noma, but which occurs in a totally different class of patient, is **phagedæna**. The ulceration which occurs in such cases spreads with great rapidity, as in the male, and is generally associated with the presence of, or has started from, soft venereal sores occurring in a debilitated patient.

A somewhat special condition is that occasioned by obstruction of the ducts of Bartholin's glands. A localised swelling is produced which is liable to become inflamed and may go on to suppuration. Swellings of this kind form one variety of labial cyst.

The labia may also be the seat of varicose veins in which thrombosis is liable to occur, particularly after childbirth, or there may take place into the labial tissue a definite extravasation of blood which forms a thrombus. This extravasated blood may be absorbed after a certain length of time, or it may break down into pus, with the formation of a **labial abscess**. The amount of blood that may be poured out in this way into the loose labial tissue is considerable.

To **urethral caruncle** reference has already been made. This condition and **carcinoma** form the principal new-growths of the vulva. Mention must, however, be made of certain enlargements of special portions. Thus one may meet with an **hypertrophy of the clitoris** which is sufficient to make it resemble a small penis. This enlargement is due to an excessive development of the spongy tissue of the organ and is of the nature of a hyperplasia. The condition must not be confounded with that in which one has to do with a malformation where the individual is really male, but simulates the female owing to the existence of a complete hypospadias, a cleft scrotum, and undescended testicles. In another form of hyperplasia there is an enlargement of the nymphæ, so that they project beyond the labia majora. This condition is uncommon in the case of whites, but may almost be regarded as normal in negroid races. An enlargement that may affect one labium or the entire external genitals is that which depends upon congenital lymphangeiectasis, and which is therefore analogous to macroglossia and macrocheilia. The enlargement may be considerable. Some authors describe the change as a cystic or cavernous lymphangeioma, and therefore include it among the true tumours. The affected tissue undergoes a change which often causes it to resemble that constituting elephantiasis.

(2) THE VAGINA

With the exception of that inflammation which depends upon gonorrhœal infection the vagina is not particularly liable to be the primary seat of disease. It is, however, frequently affected secondarily when there is disease of the vulva or of the uterus, and particularly of the cervix uteri.

Vaginitis or **colpitis** may be acute or chronic, and it need not of necessity depend upon gonorrhœa, although gonorrhœa is by far the commonest cause. Thus it may result from the irritation of a pessary or of threadworms or other animal parasites, and so forth. In the acute variety the mucous membrane is reddened and swollen, the folds are prominent, and many of them are straightened out, and there exudes from the surface a turbid fluid which consists partly of desquamated epithelial cells and partly of pus cells. Sometimes definite erosions or ulcers are present. In the chronic variety the mucous membrane may be reddened or brownish in colour from the deposition of altered blood pigment, and may be smooth or granular, or may show the presence of localised white patches which consist of heaped-up epithelium. In some of the severer cases of exanthematous disease, the lining membrane of the vagina may be covered by a false membrane similar to that which occurs in the pharynx in cases of diphtheria. True diphtheria is very occasionally found to occur in connection with the female generative organs, but then it usually affects the vulva, and only extends to the vagina secondarily. When any intense inflammatory process has been at work, recovery is associated with the formation of a large amount of cicatricial tissue, which will certainly lead to a stenosis of the vagina and may lead to its complete closure. A similar condition may result when a portion of the vaginal wall has sloughed, as the consequence of inordinate pressure during a difficult labour.

The most important new-growth of the vagina is carcinoma, but it is rarely primary. Most generally it is secondary to carcinoma of the cervix. Nevertheless primary carcinoma of the vagina is known, and it occurs as a more or less annular ulcerated growth, which is at first confined to the wall of the part, but subsequently invades the surrounding tissue and spreads upwards and downwards in the vaginal wall itself. It is of the squamous-cell variety.

One of the most important morbid conditions of the vagina is that in which it becomes involved by carcinoma which originated insome other part, such as the rectum or the cervix, and which, by its extension, leads to the establishment of a fistulous opening between the bladder and the vagina, or the vagina and the rectum, or all three of these parts. Although it is commonest for such a fistulous opening to depend upon malignant disease, it is not necessary. A communication between the vagina and the rectum, for example, may result from the sloughing of a portion of the vaginal wall in a case of protracted and difficult labour, in which the fœtal head has pressed, for a long time, the posterior wall of the vagina and the rectum against the sacrum.

(3) THE UTERUS

Atrophy of the uterus is principally seen as a senile change. The organ is smaller than normal, its walls are thinner and more fibrotic, and the internal lining is often diminished to a considerable degree in thickness. The actual dimensions of the uterine cavity may or may not be reduced. The general diminution in size affects the cervix, which is often found to project far less than normally into the vagina, and, in some instances, has atrophied to such an extent that the os forms an opening at the summit of a dome-like roof of the vagina. Under other conditions than those which constitute senility, atrophy of the uterus does not often occur. Nevertheless there is often found a localised atrophy of a portion of the uterine wall in cases in which a tumour has pressed upon a certain part and has induced a pressure atrophy. Occasionally, too, after parturition, the process of involution may go on so far that the resulting size of the organ is less than normal.

Hypertrophy and hyperplasia of the muscular tissue of the uterus are, of course, natural accompaniments of pregnancy, but with this we have not to deal here. Under other conditions a general hypertrophy does not occur. The utmost that we find is a more or less localised enlargement of the uterine wall at any part which is associated with some morbid condition. Thus, when the uterus is the seat of leiomyomata, it is common to find the organ enlarged, not only because of the presence of the tumour itself, but also because the uterine wall in places has taken on an increased growth. An enlargement which depends upon a deficiency of the changes which occasion the return of the uterus to its normal size after pregnancy (**sub-involution**) cannot, of course, be included in the present category.

Inflammation of the uterus is one of the most important of all the morbid conditions that affect the female generative organs. The inflammation chiefly concerns the lining membrane of the organ and therefore constitutes **endometritis.** Nevertheless, true metritis is always present to a certain extent in all cases of endometritis.

Endometritis may affect the body of the uterus and the cervix, or it may affect the cervix alone; in the latter case it is sometimes known as **endocervicitis.** The inflammation may be acute or chronic, and the latter is the commoner variety.

The changes which occur in endometritis are similar to those which occur in any mucous membrane. There is a reddening of the lining membrane of the uterus, with a swelling of the most superficial parts, a desquamation of the epithelial cells lining the tubular glands, and the outpouring of a large amount of mucous secretion. The normal secretion of the cervical glands is tenacious and slimy, while that of the glands in the body of the organ is more fluid and poorer in mucin. When endometritis occurs the characters of the secretion depend largely upon the particular portion of the uterus which is principally affected, as well as upon the question whether the inflammation is acute or chronic. When the inflammation is acute the secretion is generally largely mixed with thin fluid that has exuded from the blood-vessels, and it may contain blood corpuscles in sufficient numbers to cause it to appear bloody. But when the inflammation is chronic, there is a smaller probability of the presence of blood corpuscles, except those migrated leucocytes that constitute pus cells, and an altered secretion is present in a larger proportion. Hence in chronic endometritis the discharge from the uterus is white, tenacious, and copious, contains a large amount of mucus, great numbers of desquamated columnar and squamous epithelial cells, and a fair number of pus cells. It must, however, be mentioned that the alteration of the lining membrane of the uterus in cases of endometritis is generally such that conditions of **menorrhagia** or **metrorrhagia** are produced. In these conditions we have a discharge of blood from the uterus consisting in an undue prolongation and profuseness of menstruation in the first instance, and in a copious discharge of blood from the uterus at times not coinciding with menstruation in the second.

In chronic endometritis the endometrium may be altered in a number of different ways, but they all agree in the fact that there is at one time or another an increase in the thickness of the endometrium. In the majority of cases this increase in thickness persists throughout the entire duration of the condition, but sometimes there follows upon the chronic inflammation an atrophy of the endometrium which may almost amount to its complete disappearance.

The chronically inflamed endometrium is generally intensely red and swollen. It contains a large number of newly formed capillary blood-vessels and connective tissue of a loose kind, in the meshwork of which is held a quantity of œdema fluid and a varying, but usually considerable, number of extravasated leucocytes and red corpuscles, together with young fibroblasts. This increase in the thickness of the endometrium is sometimes general, so that the cavity of the uterus becomes filled up by an even encroachment from all sides; but in other instances there is a polypoid condition of the endometrium. Hence the **atrophic**, the **hyperplastic**, and the **polypoid** or fungoid varieties of endometritis have been recognised.

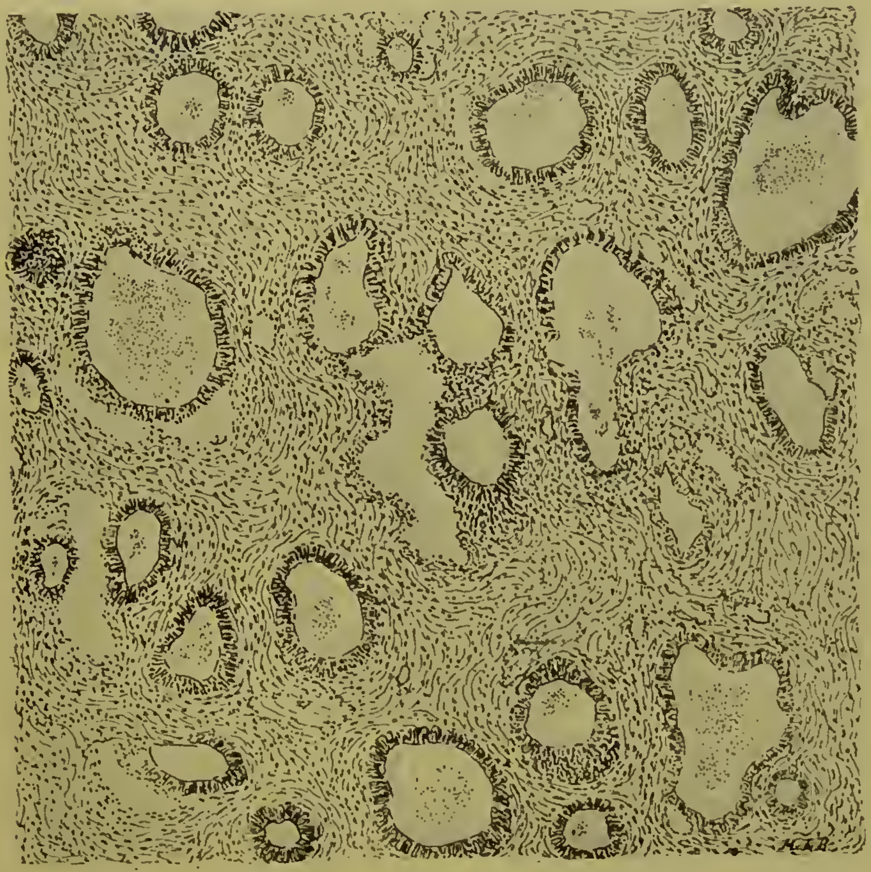


Fig. 144.—Section of Chronic Endometritis (Hyperplastic or Catarrhal Variety). × 60.

The section shows a very loose and highly cellular connective-tissue stroma with numerous somewhat irregular tubules. These tubules are lined by a layer of columnar epithelium, which is generally single, but which in places shows a tendency to proliferate.

The microscopical appearances of an endometrium which is the seat of chronic inflammation are very variable, but the tubular glands are always profoundly altered in cases of long standing. They become elongated, the epithelial cells which line them undergo a most pronounced proliferation, and the tubules themselves become tortuous and frequently branched at their internal extremity. The result of these changes is that in a section we find a more or less loose tissue in which there are present numbers of large, somewhat irregular, duct-like spaces, which are lined by a columnar epithelium that shows, in places, a tendency to proliferation. Such appearances are very closely similar to those of a columnar cell-carcinoma.

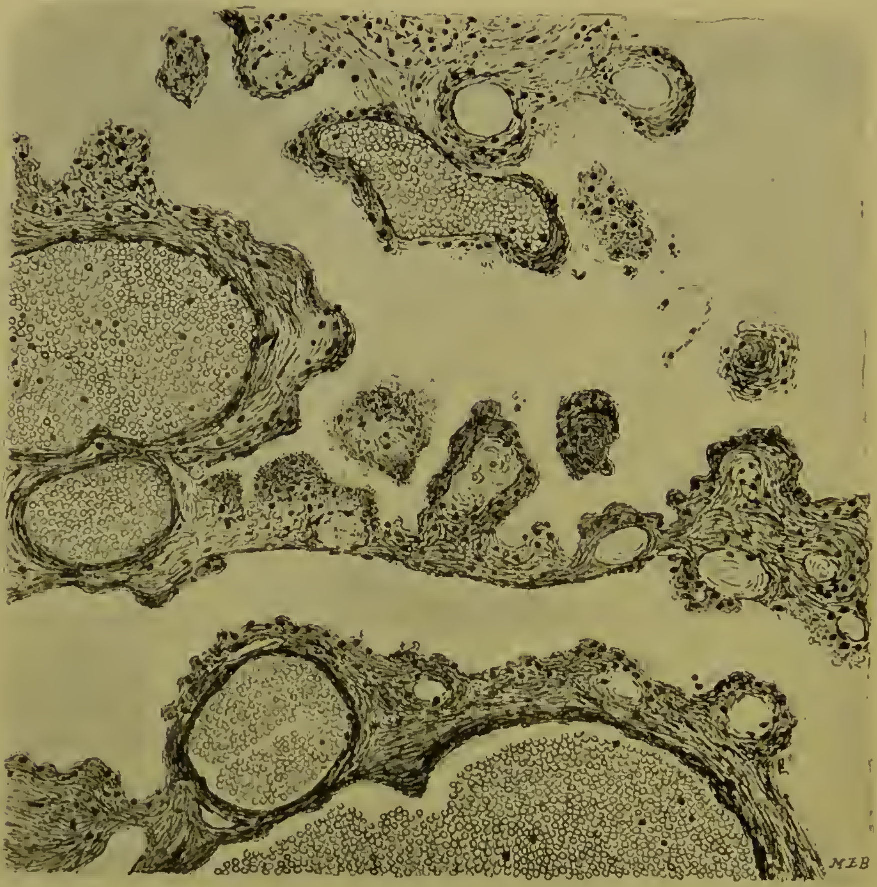


Fig. 145.—Section of Chronic Endometritis (Polypose Variety). × 420.
Numerous papillomatous projections are cut in section. The most important characteristic is the number of relatively large blood-vessels that run in the projections. Parts of the 'polypi' other than the vessels show a loose highly cellular fibrous tissue with a certain number of tubular glands of small size.

Great variations are also seen in the amount and character of the intertubular stroma. In some cases there is a relatively large amount of newly formed fibrous tissue, with but few tubular glands, and few cells other than fibroblasts; in other cases the number of cells pervading the connective-tissue framework is so considerable that it almost appears to be of a sarcomatous nature, while the glands are found in great numbers. The degree of vascularity also varies within wide limits. As a rule the number of small young blood-vessels is considerable, and there may be evidences that a great deal of extravasation of blood has taken place into the inflamed membrane during life.

In association with endometritis, but also sometimes apart from that condition, it is common to meet with alterations both of the glands that lie within the cervix, and of the epithelial covering of the vaginal portion of the cervix. In the former case there occurs an obstruction of the orifices of some of the endo-cervical mucous glands, with the production of retention cysts. These cysts stand up as small oval swellings with translucent contents and are known as **ovulæ Nabothi**. Sometimes the fluid contained in these cysts is purulent. In the latter instance we have to do with an **erosion**.

An erosion of the cervix is constituted by a localised loss of a portion of the epithelial covering of the part. The epithelial lining of the uterus is composed of columnar cells, and this form of lining persists as a rule over the upper two thirds of the cervix. But the lower third of the cervix is lined internally by a squamous epithelium continuous with and similar to that which covers the whole of the vagina and the outer surface of the cervix. Sometimes in the course of an endometritis this lower portion of the cervix becomes extroverted (**ectropion**), and the epithelium over it becomes macerated, and desquamates, with the production of a localised patch, which is either invested by a much thinner layer of epithelium than elsewhere, or is denuded of epithelium altogether. Such epithelium as remains is generally of a columnar type. Owing to the thinness of the epithelial covering, an erosion is of a bright red colour and bleeds very easily. Sometimes the surrounding tissue becomes papillomatous, and even if definite papillomata do not form, the surface of the erosion is likely to be irregular from the presence on it of the open mouths of the mucous glands. Although an erosion is distinct from an ulcer in its characters, and to a large extent in its method of formation, it may terminate by the formation of a definite ulcer. Erosions are apt to be accompanied by the presence of small cysts in their neighbourhood, and in many instances the erosions are due to the breaking down of the small amount of epithelial tissue which lies superficial to the cyst.

It is probable that erosions are of very common occurrence, quite apart from endometritis. At all events they are not uncommonly found in the case of virgins in the *post-mortem* room.

The histological characters of a cervical erosion will have appeared largely from the foregoing remarks. As a rule, one finds that there is present an irregular surface which consists largely of a loose connective tissue, in the meshwork of which are large numbers of leucocytes, and that at various parts of this there open the mouths of tubular mucous glands. Large portions of the epithelium have disappeared, and such as remains is at some places of the columnar type, at others of the squamous.

The causes of endometritis are various, but in the vast majority of cases the condition may be traced to the introduction of micro-organisms (particularly streptococcus pyogenes, staphylococcus pyogenes aureus, micrococcus gonorrhœæ) from without. To the activity of these micro-organisms some condition of the endometrium may contribute. Thus the uterus may have just passed through the changes incident to pregnancy and parturition, and some portions of the fœtal membranes or placenta or blood-clot may have been left behind, or the uterus may be the seat of a new-growth such as a fibromyoma or a polypus, or it may be senile. Under any of these circumstances the endometrium is in an unhealthy condition, and affords a ready nidus for the growth of bacteria. In some cases, however, the explanation of the inflammatory condition is quite uncertain.

So far as the other varieties of inflammation are concerned there is but little to say. **Syphilis** may affect the cervix, either as a primary sore or as a gummatous or condylomatous mass. In either instance the appearances are not different from those obtaining elsewhere. The same is true of syphilitic endometritis.

Tuberculous affections of the uterus are somewhat uncommon, although similar affections of the uterine appendages are seen with fair frequency, as will be mentioned hereafter. It is a question of doubt whether uterine tuberculosis is ever the result of an extension of tuberculosis from the lower part of the generative tract. That it is, in the vast majority of cases, due to extension from disease of the ovaries or tubes, there is no doubt. In tuberculosis of the uterus we may find that the tuberculous nodules are present in the endometrium or in the wall of the uterus itself. Under either circumstance the tuberculosis is of an extremely caseous type, so that the ultimate result is the presence of a large amount of caseous material in the cavity of the uterus which replaces to a greater or a less amount the uterine substance itself. So much is this the case that the uterus is perhaps represented by a thin-walled sac containing thick caseous material, the whole being as large as a chestnut. Uterine tuberculosis is most generally seen in children, and is associated with tuberculous peritonitis.

New-growths.—The only kinds of new-growth that are of considerable frequency are leiomyomata and carcinomata.

Leiomyomata, whether pure or combined with so large an amount of fibrous tissue that they deserve the clinical name of 'fibroids,' constitute the commonest form of new-growth affecting the uterus. It is customary to divide them into three classes, according as they are situated most closely towards the peritoneal covering of the organ (sub-peritoneal) or the endometrium (submucous), or are situated in the thickness of the uterine wall itself (interstitial). In one sense every fibromyoma is interstitial in that it commences as such, but its subsequent nature depends upon the question as to whether its growth takes place more in the external or the internal direction.

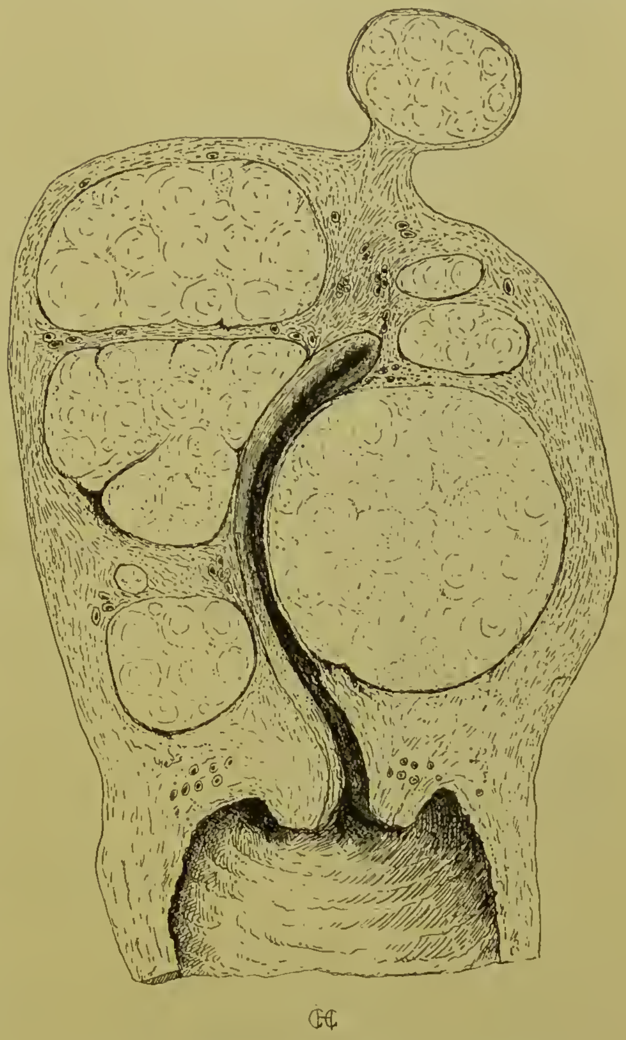


FIG. 146.—UTERUS SHOWING MULTIPLE FIBRO-LEIOMYOMATA. × ½.

The specimen shows a sub-peritoneal, several interstitial, and two submucous fibroids. The uterus itself is enlarged and the cavity elongated.

A uterus which is the seat of fibromyomata (for they are generally multiple) is always enlarged unless the tumour is frankly sub-peritoneal, and even then some enlargement is frequently observed. The ultimate shape of the organ and of the uterine cavity is very variable, but the entire mass may be as large as a man's head. The presence of uterine fibroids is always accompanied by a greater or smaller degree of endometritis, and it is the hæmorrhage from this altered endometrium that accounts for the loss of blood which is an important symptom of the disease.

During its growth a uterine fibromyoma may become pendulous and form one variety of uterine polypus. As a rule these polypi are small and are attached to the uterine wall by a definite pedicle, but in other cases the pedicle is so thin that the tumour ultimately becomes separated, and thus the condition spontaneously cures itself. A similar separation of a pendulous fibroid with a delicate pedicle occasionally occurs also in the case of sub-peritoneal tumours, and then the detached growth may lie innocuous in the abdominal cavity, or it may contract adhesions and fresh attachments with some other part, such as the omentum. In the case of a submucous fibroid, insufficiency of nutrition and superficial irritation may combine to produce a necrosis of the growth. If, under these circumstances, the amount of necrosed tissue is considerable, the resulting putrefaction may be accompanied by very severe symptoms.

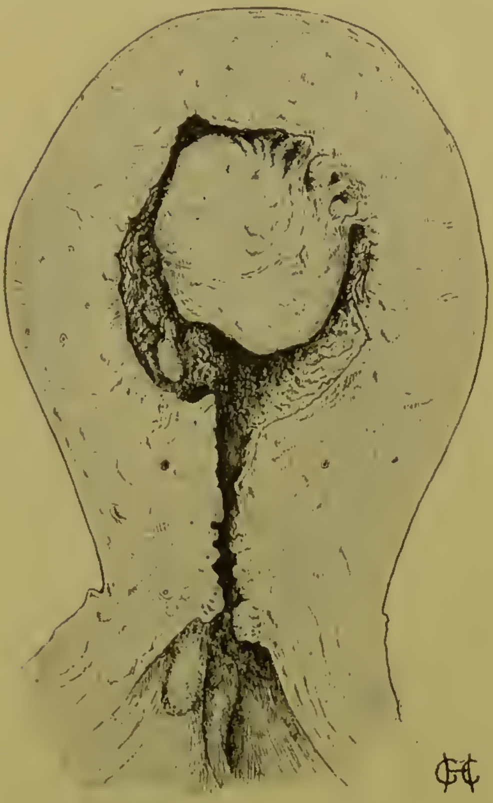


FIG. 147.—MALIGNANT DISEASE OF THE BODY OF THE UTERUS. × $\frac{3}{4}$.

The cavity of the uterus is enlarged and its walls ragged. At the fundus the new-growth has formed a polypoid mass. The case was one of spheroidal-cell carcinoma.

Pendulous fibromyomata form one variety of uterine polypus, but pure fibromata may form another variety. Neither of the two, however, constitutes the larger number of polypi, which consist of œdematous and hyperplastic mucous membrane which has become provided with a pedicle and springs from the cervical canal. The other varieties of polypus generally originate from the body of the uterus, although they may present at the external os.

Carcinoma of the uterus is sharply divided into two varieties, according as it affects the body of the uterus or the cervix. Of these two varieties, carcinoma of the cervix is far the more common.

Carcinoma of the body of the uterus may manifest itself either as a general alteration of the endometrium, associated with ulceration, or as a prominent growth or growths springing from a definite region and filling up the uterine cavity. Carcinoma of the cervix, on the other hand, generally appears as a local growth on one lip of the external os, and spreads thence into the cervical canal and into the fornices of the vagina, until it involves the entire os and the surrounding tissue. In both instances the growth commences in the lining epithelium and invades the muscular coat subsequently. When the growth has extended to a certain point, it generally undergoes a superficial molecular necrosis.

In course of time the degree of destruction that is produced by the growth of the cancerous mass may become very considerable, and the upper end of the vagina may be filled with a fungating mass that bleeds at the slightest touch, and is nevertheless hard in places where the destruction has not, as yet, proceeded to any great extent. Not infrequently the mass, in cases of cervical carcinoma, has a cauliflower appearance. When the growth extends backwards, it often leads to the formation of a recto-vaginal fistula; when forwards, to a vesico-vaginal fistula. The appendages and the neighbouring peritoneum are liable to become involved in a hard cancerous mass. The pelvic lymphatic glands may also become secondarily affected. In a few cases carcinoma of the body is evenly spread throughout the inner lining of the uterus, and does not extend further. In such cases cursory examination of the endometrium or uterus may cause the nature of the disease to be completely overlooked.

(4) THE FALLOPIAN TUBES

The only changes which it will be necessary to mention are those which constitute different forms of inflammation and their results.

Acute inflammation of the Fallopian tubes (**salpingitis**) is of fairly common occurrence. Its general cause is an extension from an inflammatory condition of the endometrium, and hence the chief form of salpingitis is that which is dependent upon the gonococcus. Indeed, gonorrhœa is accountable for the vast majority of all the inflammatory affections of the uterine appendages.

In acute salpingitis the Fallopian tubes are considerably swollen, so that the lumen is often discoverable only with the greatest difficulty. The tubes themselves may be as thick as the little finger, and all the coats, as well as the mucous membrane, are involved. The mucous membrane itself is swollen, congested, and œdematous. Frequently the lumen of the tube contains a small amount of a tenacious turbid mucus, but when the condition has proceeded beyond the initial acute stage, and has become somewhat chronic, there is a definite formation of pus. In a marked case the inflammation of the serous membrane is accompanied by the formation of a fibrinous 'false membrane' on the outer surface of the tubes, and when this is the case the inflammatory process is generally found to be spread further over the peritoneum. The fimbriated ends of the tubes are always markedly altered, being deeply congested, œdematous, and often involved in a localised peritonitis.

Microscopically, the changes in acute salpingitis are those of an acute inflammation of a mucous membrane, combined with the extension of those changes to a muscular and a serous coat. Thus the mucous membrane is swollen and infiltrated with leucocytes, the epithelial cells are in many places proliferated, in many desquamated, while the entire mucous membrane is thrown into folds to a more conspicuous extent than normal, owing to its own increase in bulk, and the changes which have occurred in the muscular coat. There may be some evidence of hæmorrhage into the mucous membrane, but this is not very usual; on the other hand, the blood-vessels are generally conspicuously congested. The muscular coat shows the presence of a large number of migrated leucocytes in the connective tissue between the individual muscular fibres, and as a result of this infiltration and the swelling of the muscular fibres themselves, the thickness of the entire coat is increased. The connective tissue lying immediately beneath the peritoneum is œdematous, and contains a fair number of leucocytes, but they are generally less numerous than towards the lumen.

Chronic salpingitis is but a sequel to the acute variety, and resembles it macroscopically, excepting that the enlargement of the tube is rather due to the presence of an increase in the amount of fibrous tissue than of the cellular accompaniments of acute inflammation. Nevertheless the number of leucocytes found in a chronically inflamed Fallopian tube is always much greater than that normally present. This is owing to the fact that the secretions within the lumen are still of such a kind as to occasion outbreaks of acute inflammation from time to time.

When an acute salpingitis has led to the formation of much pus, it is probable that the pus will collect in the tube and form a somewhat specialised form of abscess (**pyosalpinx**). The reason of this is partly that the uterine orifice of the tube is normally very small, and, as the result of the swelling of the mucous membrane, becomes completely obstructed, and partly that the inflammation leads to the formation of definite fibrous septa across the lumen of the tube. As a result, the entire tube may be dilated until it forms a sausage-shaped tumour of considerable size that can be easily felt on vaginal examination. In cases of chronic inflammation, where the uterine and the abdominal orifices of the tube have become closed, the result is sometimes the formation of a similar cyst, which contains a clear fluid and constitutes a **hydrosalpinx**. The extent to which a hydro- or pyosalpinx is surrounded by adhesions resulting from a local peritonitis depends upon circumstances and differs greatly in different cases. Sometimes it is difficult to determine whether the collection of fluid found in the midst of a mass of newly formed fibrous tissue is or is not the altered Fallopian tube, in other instances such adhesions are practically wanting.

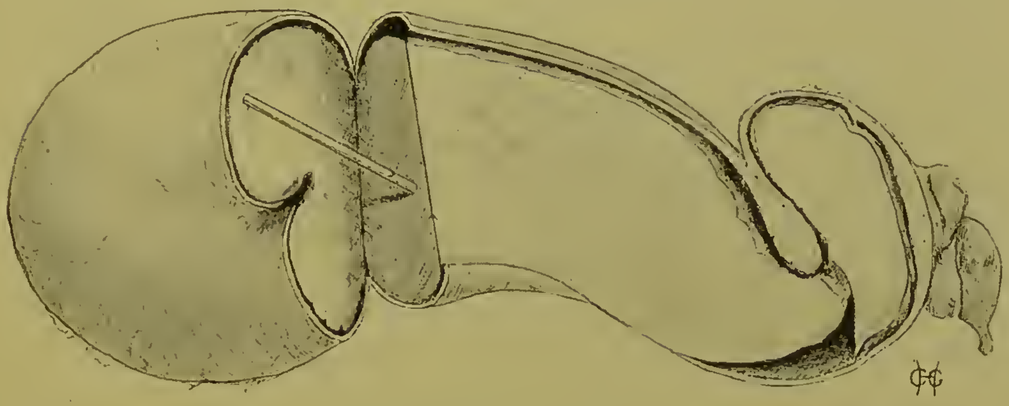


FIG. 148.—PYOSALPINX. × $\frac{3}{4}$.

A pyosalpinx which has been partly cut across in two planes to show the contents. The solid character of the contents and the contraction at the left-hand end of the sac are due to processes of preparation.

In addition to the above, the condition known as **hæmatosalpinx** is also sometimes met with. This condition may be dependent upon a very acute inflammation of the tube, in which the secretion contains so large a number of blood-cells that it practically consists of pure blood, or it may depend upon a tubal gestation which has ruptured before reaching to so large a size that the entire tube ruptures. In either case the contents of the cyst are largely composed of blood-clot.

The only other variety of salpingitis which need be mentioned here is the **tuberculous**. It occurs in combination with tuberculosis of other parts of the internal generative organs, particularly the ovaries, and is often only a secondary and subordinate part of a tuberculous peritonitis. Nevertheless the condition may be found in connection with the generative organs alone. In accordance with the points that have been mentioned, we find that tuberculous salpingitis may affect either young children or young adults. Under any circumstances the condition is never found to affect the tubes exclusively, and there is always a large amount of inflammatory fibrous tissue around the altered tubes. As a matter of fact, the pelvic organs in such cases are generally found to be matted together into an inextricable mass which consists principally of newly formed, but very dense, fibrous tissue, in the midst of which is found a number of softened foci containing a creamy purulent fluid. In the case of the adult, it is often extremely difficult, or quite impossible, to determine whether the pelvic condition depends upon tuberculosis, or whether it is due to an inflammation, such as that caused by gonorrhœal infection, which has extended to the tubes from below and has led to a local inflammation of the peritoneum.

(5) THE OVARIES

Atrophy of the ovaries is a normal accompaniment of old age, but it may occur before the climacteric as the result of inflammatory changes such as will be described immediately. The atrophied organ is always smaller than normal, and shrunken, as a rule, with irregular cicatricial foci on the surface, but the diminution in size may be regular, with the result that the surface of the organ is smooth. On section there is a considerable increase in the amount of fibrous tissue, with the presence of a number of whitish foci which are apparently the remains of former corpora lutea or Graafian follicles.

Inflammation of the ovaries (**oophoritis**) may be acute or chronic, and in a few cases it may terminate in the production of ovarian abscesses. In almost all cases the ovarian condition is due to an extension of an inflammatory process which has commenced in the uterus and has extended thence by way of the Fallopian tubes to the ovaries. For similar reasons there is almost always present a certain amount of local peritonitis which binds down the ovaries in the broad ligaments and attaches them closely to the abdominal ends of the tubes. In the acute varieties this peritonitis is associated with the presence of a large amount of fibrin, but in the chronic varieties the adhesions are composed of fibrous tissue which is frequently of an extreme density. In cases in which there is suppuration, the formation of pus may affect the ovary alone, so that a definite abscess is formed in the substance of the organ ; but in the majority of cases the process is far more widely spread, with the result that there is a general matting together of the tissues in the pelvis, and particularly in Douglas's pouch, and the presence of a number of foci of suppuration at different points, amongst which the ovaries have to be reckoned.

The histological characters of simple oophoritis are difficult to determine, owing to the infrequency with which specimens are obtained which show an inflammation uncomplicated by adhesions or suppuration affecting parts other than the ovaries. In advanced cases there is a great disorganisation, so that little if any ovarian tissue is left, its place being taken by newly formed fibrous tissue in the meshwork of which are collected numbers of leucocytes. In cases that are obtained very early the ovary is definitely reddened and swollen, and sections show the presence of congestion and leucocytic infiltration. Frequently, in the very early and very acute cases a thick layer of fibrin derived from the inflamed peritoneum forms an envelope for the ovary which can be stripped off with comparative ease.

Very variable appearances are given to the ovary, at times, by the different forms which the **corpora lutea** may assume. At their moment of formation they constitute definite hæmorrhagic foci in the substance of the ovary which are generally excentric, and reach up to the surface of the organ at some point. As time goes on they are liable to undergo retrogressive changes, of which the commonest is a disappearance of the hæmoglobin, with a formation of what appears to be a capsule enclosing thick white or yellow homogeneous material. Ultimately such a condition gives place to the formation of a cicatrix, numbers of which are generally to be found on the surface, and in the substance of an ovary derived from the body of a woman of middle age. But sometimes it is found that the corpus luteum has become cystic, and then there is present a capsule which contains either watery or creamy contents, and the entire focus may constitute as much as one half of the bulk of the ovary. Unless these appearances of the corpora lutea are recognised, it is easily possible to mistake the condition for a localised tuberculosis.

The **new-growths** of the ovary are various, but amongst the non-malignant growths the commonest is fibroma, and amongst the malignant growths the commonest is sarcoma. A very important variety of new-growth is that in which cysts are formed, and in some of these, where the epithelial lining undergoes proliferation, the resulting condition is one of a carcinomatous type.

Fibromata of the ovary are not very common. As a rule, too, they do not reach to a considerable size. Most commonly they are less than a walnut in size, and are of intense hardness. Sometimes, however, they are much larger; in the museum of the Westminster Hospital is one nearly as large as a man's head. When the growths are as large as this, however, they have generally passed out of the category of simple fibromata into that of spindle-cell sarcomata.

The **sarcomata** of the ovary may consist of spindle cells, or they may be composed of irregular and mixed varieties of cell. As a rule, the growth is circumscribed and keeps the normal shape of the organ to a great extent, although there is much enlargement. They may undergo myxomatous degeneration in places, with the formation of cysts.

The **cystomata** of the ovary (and along with them we may consider the carcinomata) constitute the most important new formations of the organ, as well as the most common. They may be simple or compound, non-malignant or malignant, large, so that by reason of this very factor they constitute a danger to life, or so small that they are of no clinical importance.

Simple cysts of the ovary are those which it is believed arise from a dropsical distension of normal Graafian follicles. In a minor degree such a condition is known as **hydrops folliculi**, and it may lead to the production of a cyst, perhaps as large as a chestnut, but often smaller, that is provided with clear watery contents, and projects somewhat from the surface of the ovary. When such cysts are numerous the entire ovary may be converted into a multilocular cystic formation. Reference has already been made to the ovarian cysts that originate in corpora lutea.

A variety of cyst which is frequently considered as distinct is the **tubo-ovarian**. Tubo-ovarian cysts are always shaped somewhat like a retort, and they may reach to a fairly considerable size. They contain a clear fluid, and sometimes are unilocular, sometimes bilocular, owing to the presence of a septum dividing the abdominal opening of the tube from the ovarian cyst. As a matter of fact, it is now generally believed that the tubo-ovarian cyst is nothing more than a somewhat special variety of a hydrosalpinx, in which the peculiar form is due to the fact that the abdominal opening of the tube has become closed, and has, at the same time, contracted adhesions to the ovary itself.

Another variety of simple cyst met with in this region is the **parovarian**, which arises in one of the tubes of the parovarium, and which, by its close contiguity to the ovary, may give rise to the impression that it is ovarian, although, in reality, it is situated between the layers of the broad ligament. Parovarian cysts are always unilocular, and may reach to a very considerable size. They are provided with a firm wall which is lined by a regular layer of flattened epithelium, and they usually have watery contents, though these may, on occasions, be reddish or brownish from the presence of small admixtures of altered blood.

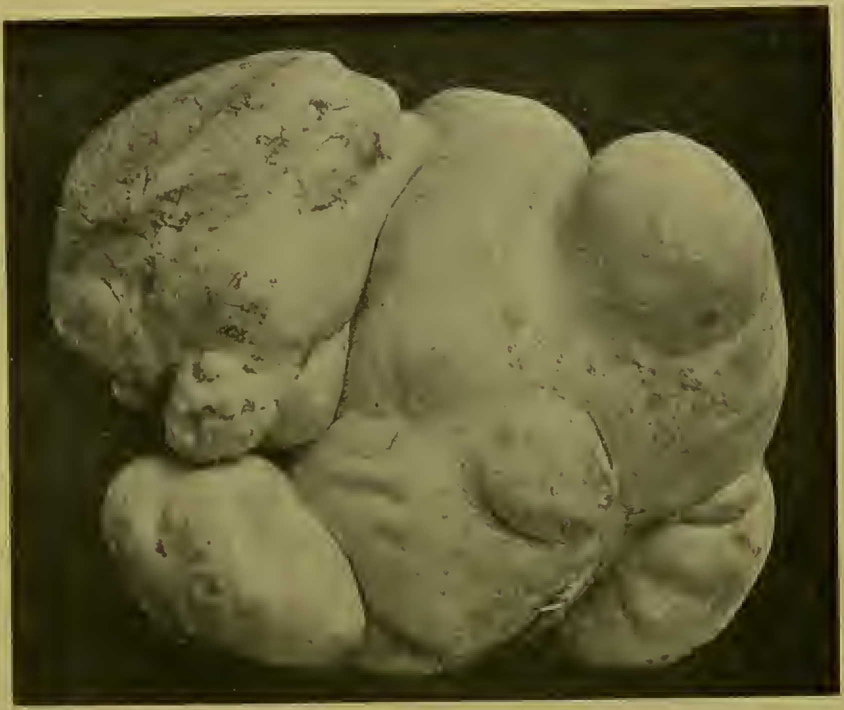


Fig. 149.—A Multilocular Ovarian Cyst. ×. $\frac{1}{3}$.

The cyst weighed 23 lbs. and contained mucilaginous fluid. A few adhesions were present between it and the neighbouring parts, and portions of these are seen particularly over the left upper cyst.

True cysts of the ovary are practically always multilocular, and they vary considerably in appearance. Sometimes the cysts are filled with a watery fluid, but in most cases the contents are viscid from the presence of large quantities of paramucin. The contents may also be colourless, or of a red, brown, yellow, or greenish colour. The cysts themselves vary considerably in size, a fairly large one weighing, with its contents, about fifteen pounds, but they have been described as weighing one hundred pounds.

The principal difference between the varieties of multilocular ovarian cyst lies in the question as to whether there is or is not present a tendency to the formation of intracystic papillary growths. That variety in which the formation of intracystic papillary growths is a prominent feature calls for special description.

In all cases of multilocular cyst the individual cysts are lined with epithelium. This epithelium is generally very regular and is of the columnar type, whether the cells are long or flattened; occasionally the epithelium is found to be ciliated. Even in typical multilocular cysts it is common to find situations in which there is a tendency for the wall of the cyst to be projected into the cyst cavity, and these, being covered with epithelium, constitute small inconspicuous papillomata. In the truly **papilliferous** or **proligerous** ovarian cysts, however, this tendency to the formation of intracystic papillomata is carried to a great extent. It is not necessary that it shall affect all the component cysts, though it is general to find that in some degree the formation of papillomata obtains everywhere. But in those in which it is well marked the entire cavity of the cyst is filled by a number of greatly branching papillomatous formations, which leave so little room for any fluid cystic substance that the cyst so affected frequently appears to be solid.

In those cases in which the intracystic formation of papillomata is very pronounced, the rate of growth may be so rapid that the cyst wall ruptures, and the growths commence to sprout within the peritoneal cavity freed from any restraining influence. At the same time small portions of the papillomata may be broken off, and become engrafted upon distant parts, where they continue to increase in size. It is this feature of the papilliferous cysts of the ovary which has earned for them the name of **malignant**, for they ultimately destroy life. The epithelium covering the papillomata also shows a certain degree of atypia, so that they approach somewhat closely to the true carcinomata.

So far as the multilocular cysts of the ovary themselves are concerned, they are probably to be included amongst the adenomata, in that they probably develope from the epithelium of the follicles, or at all events from duct-like formations or tubular glands. How far the superficial germinal epithelium takes a share in their formation is unknown.

In addition to the carcinomatous adeno-cystomata, the ovary is sometimes the seat of a solid carcinomatous tumour, which does not differ greatly in its appearances from similar tumours met with elsewhere. Histologically, these tumours may be of the spheroidal-cell or of the columnar-cell type, and they may even show some tendency to the formation of villi, but this is infinitely less common than in the case of the carcinomatous adeno-cystomata, which always show a pronounced tendency to the formation of villi. Portions of the growth, and particularly of the stroma, may undergo degeneration, as the result of which the tumour may become myxomatous or, in rare cases, calcareous.

The ovary is also liable to be the seat of dermoid cysts. These vary considerably in size, but the majority are about as large as a hen's egg. The wall consists externally of fibrous tissue, with an internal portion which consists of a modified epidermis. Agreeably with this structure there are found in the wall those elements which are present in normal skin, viz. sebaceous glands and hair follicles with hairs, and sweat glands. Occasionally, too, teeth are implanted on the cyst wall, and they may be arranged in a piece of bone which bears a superficial resemblance to a jaw. The contents of the cysts are principally sebaceous material and hair, but other formed elements belonging to the connective-tissue series are sometimes also present. The hairs are always of a very light colour, and they may be very scanty or present in so large numbers that they constitute the principal object within the cyst.

(6) MALFORMATIONS

In spite of the intricate nature of the processes concerned in the development of the generative organs, malformations of the female genitals are not very common. Perhaps the commonest condition is that in which the hymen is imperforate. As a result of this condition when puberty arrives there is no outlet for the menstrual fluid, and it accumulates within the uterus and vagina, distending them, and itself becoming altered until it is as thick as tar and has a deep chocolate colour. The condition then forms one variety of 'hæmatometra.'

Another form of malformation which is also uncommon is that in which the uterus, and perhaps the vagina, still shows evidences of its bipartite origin. The commonest condition is that in which the uterus is cornuate, and then there may be two horns corresponding to the origins of the Fallopian tubes, or one horn, the other tube being aborted. A condition in which the entire internal generative system is double has been occasionally met with, but is excessively rare. Other malformations of the generative tract occur, such as absence or a bipartite condition of the vagina, a bilocular condition of the uterus, absence of the ovaries, &c., but they need not detain us here. Although the condition is hardly a malformation, it may be said that occasionally the generative organs fail to undergo the normal changes at puberty. The result is that the infantile condition persists, although there occurs a certain amount of general increase in size commensurate with the general growth of the body. In cases such as these it is important to be certain that the individual is really female, and is not a male with hypospadias and undescended testicles, which constitute appearances mistaken for those of a female. Such a mistake is very liable to be made.

(7) PATHOLOGICAL CONDITIONS INCIDENTAL TO PREGNANCY AND PARTURITION

It would be impossible to enter into a complete account of the pathological conditions which may fairly be included under this heading, partly because of their numbers and diversity, and partly because many of them are but little known or understood. Reference will therefore be made here only to those which are of more common occurrence.

The subject naturally divides itself into conditions which affect the maternal and those which affect the fœtal structures. Nevertheless in many instances both of these become involved.

(*A*) **The maternal tissues.**—The principal morbid conditions which affect the maternal structures are those which occur during parturition and subsequently. Amongst these must be mentioned lacerations that involve the uterus, such as that which occurs at Bandl's ring and produces the formidable accident of rupture of the uterus; lacerations of the cervix or of the vagina, which are frequently the sites at which those micro-organisms enter that are concerned in the production of sapræmia and septicæmia; lacerations of the external genitals, particularly the labia (and the perinæum), which are accountable for the production of labial thromboses, hæmorrhages, and abscesses. Concerning these no further remarks are necessary, with the exception of the condition which is conveniently, if popularly, summed up under the name of 'puerperal fever.'

Septic conditions associated with childbirth are of two distinct kinds according as the micro-organisms which are responsible for the production of the toxic material that leads to the symptoms are themselves pathogenetic and capable of living within the animal tissues, or are saprophytic and only capable of living upon dead material which is, physiologically, outside the body. In the case of the saprophytic micro-organisms there is always present some material (blood-clot, portions of membranes, &c.) which affords food for the putrefactive bacteria that enter from the outside. In this material the bacteria multiply and form their toxins, and it is owing to the absorption of these toxins that the disease is produced. Moreover, the degree of fever, &c., varies directly with the dose of the poison absorbed, and therefore if the putrefying material is removed the disease begins to abate forthwith. The condition is one of **sapræmia.**

In **septicæmia** it is also possible that some dead material may be present, but its removal is not followed by a disappearance of the symptoms, because the micro-organisms have gained access to the tissues of the woman, and, multiplying there, form their toxins physiologically within the body. The actual micro-organisms concerned also differ in the two cases. For in septicæmia the organism is most commonly either *Streptococcus pyogenes* or *Staphylococcus pyogenes aureus*, while in sapræmia the organisms are generally the common bacteria of putrefaction and particularly different varieties of *Proteus*. A further difference between the two conditions obtains in the fact that it is very common to find in septicæmic cases a complete absence of any foreign material in the generative passages. On the other hand, there may be a fibrinous mass of indefinite composition, but principally consisting of fibrin, which is intimately attached to the uterus at some point or other, and particularly at the fundus.

So far as the actual morbid changes are concerned which are present in the body of a person who has died from an acute infection following on parturition, they are those of either a septicæmia or a pyæmia. In most cases there is a local peritonitis at least, and the peritonitis may be general. It is associated with the presence of an adhesive fibrinous deposit in Douglas's pouch and the immediate neighbourhood of the uterus. Sometimes actual pus is found, but generally this is only the case when the condition has lasted for some little time. In other parts of the body little may be found. The blood is likely to be fluid, and the intima of the blood-vessels are usually deeply stained with the dissolved hæmoglobin. Probably it will be possible to obtain a cultivation of streptococci or staphylococci from the heart's blood. A number of petechial hæmorrhages will most likely be found immediately beneath the serous coverings of the lungs and heart; in the latter instance they will be present in largest numbers about the base. In cases in which the disease has been of the pyæmic variety, abscesses of various size will be found in the internal organs, particularly in the lungs. It is commoner, however, for septicæmia to occur than pyæmia.

Amongst the morbid conditions which supervene at a later date after parturition is that which consists in a deficiency of those processes which are concerned in the return of the gravid uterus to its normal state (**sub-involution**). A sub-involuted uterus is always larger than normal and considerably softer. As a rule there is a marked degree of fatty degeneration in the muscular fibres, and this is associated with an alteration of the uterine vessels whereby a larger number of them than usual becomes obliterated.

In the case of the **placenta**, morbid conditions are not very uncommon; in their severer forms they have important bearings upon the nutrition of the fœtus. The simplest change consists in an abnormal adhesion of the placenta to the uterine wall. This may occur in persons who are otherwise healthy, although it is a pronounced result of syphilis. In simple cases it appears to be due either to an increase of those processes which tend to repair the placental site—that is, there is an undue formation of fibrous tissue at too early a date (i.e. *before* instead of *after* parturition)—or to a deficiency of the fatty changes which, accompanied by a certain amount of thrombosis, occur at the latter end of pregnancy and prepare the way for the separation of the placenta at the proper time.

Syphilitic changes of the placenta are of various kinds. One of the commonest changes is endarteritis obliterans. As a result of this process, portions of the placenta are liable to undergo fatty change and a subsequent fibrotic change; in the latter instance the placenta is extremely hard to detach from the uterine wall. Gummata are of rare, but of occasional, occurrence.

Tuberculosis of the placenta is rare, but sometimes definite tuberculous foci that have undergone caseation are found. It is probable that this condition is accountable for all cases of congenital tuberculosis.

An important morbid condition of the placenta is that in which, owing to some accident, hæmorrhage has taken place in its substance. The extravasated blood may be found in the form of definite coagula, or it may have undergone a certain amount of organisation. In the latter case the placenta is abnormally adherent to the uterine wall.

Morbid changes also occur in other parts of the decidua than the decidua serotina which goes to form the placenta. Thus it may be the seat of hæmorrhage (and this is a very important cause of abortion), or it may undergo fatty degeneration, or even calcareous deposit may take place in its substance. It may also be the seat of pronounced infiltration with small round cells, or portions of it may become fibrous; these changes are most apt to occur in cases of syphilis.

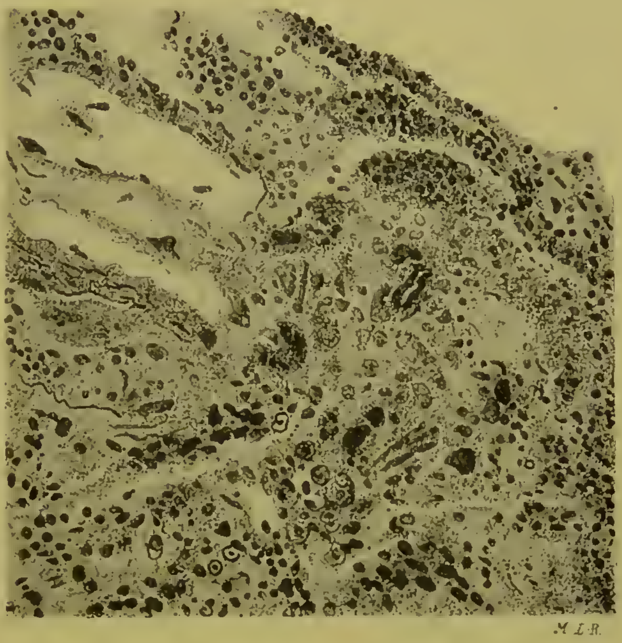


FIG. 150. — SECTION OF DECIDUOMA MALIGNUM. × 360.

The actual section was from a secondary nodule in the lung. Towards the centre are seen some of the large syncytial cells with large nuclei.

The most obvious alteration of the **chorion** is that in which the chorionic villi become cystic with the production of what is sometimes called a '**hydatidiform mole.**' In this condition the cavity of the uterus is filled with an easily broken-down material which, in mass, greatly resembles the appearance of stewed red currants. Sometimes one finds only a portion of the entire uterine contents altered in this way, but usually the uterus is filled with a mass of this description, weighing, perhaps, a couple of pounds. Rarely, it is found that a portion of the placenta has become hydatidiform, a fœtus being present; but far more commonly there is no trace of a fœtus whatever.

Another alteration of the decidua, one which has been the subject of considerable discussion, is that in which it undergoes a malignant change. The nature of this change has not yet been entirely settled. By some authors it is regarded as being of the nature of a sarcoma, and has been called a '**deciduoma malignum**' or '**sarcoma deciduocellulare.**' In any case, the condition consists in the formation of a number of polypose growths which are intimately connected with the uterine wall, which fill the uterine cavity, and, on section, show the existence of a great proliferation of the large decidual cells. These cells are chiefly found close to the uterine wall, and the bulk of the mass is made up of blood-clot and fibrin. Amongst the decidual cells are generally present large numbers of cells having smaller and fairly round nuclei. It is uncertain whether these are to be regarded as mononuclear leucocytes or as endothelial cells which have originated from the endothelial lining of the capillaries.

A point which has important bearings upon the question as to the nature of these growths is the fact that secondary nodules may be found in distant parts (e.g. the lungs) which have identical histological appearances with those present in the primary growths, including the existence of the large decidual cells. Whether, therefore, they are to be regarded as originating in maternal or in fœtal structures, there is no difficulty in classing them amongst the true malignant growths.

Extra-uterine gestation.—Into this subject, so far as it is of obstetric or of surgical importance, we shall not enter here, for important though the subject is from other points of view, it is relatively unimportant from that of pathology. It is commonest in these cases to find that the impregnated ovum becomes established somewhere in the Fallopian tube, either midway between its uterine and its abdominal ends, or close to its opening into the uterus. In very rare instances an ovarian gestation has been described, as well as a gestation which has taken place in the abdominal cavity itself, but these are merely pathological curiosities.

In a tubal gestation the muscular coat of the tube undergoes changes similar to those which occur in the uterus itself under normal circumstances. There is a marked hypertrophy and hyperplasia of the muscular fibres, with a corresponding thickening of the tube. The lining membrane also becomes altered to form a decidua, and, if the pregnancy goes on long enough before rupture of the tube, a placenta may be formed. In almost all cases the tubal gestation ends by the rupture of the tube and the expulsion of the fœtus, together with its membranes and a large amount of blood-clot, into the abdominal cavity. If the pregnancy has been of only a very short duration, the extruded fœtus, which will have ceased to live, and the surrounding blood-clot may become encapsuled within the abdominal cavity and persist for a long time without causing any trouble.

In cases of extra-uterine gestation the uterine lining membrane and wall undergo the changes incidental to pregnancy, but in a minor degree.

(*B*) **The fœtus.**—A consideration of the pathological changes which affect the fœtus would lead us into the realm of antenatal pathology, a subject concerning which but little is known. It would be necessary to consider the different varieties of congenital malformation, whether due to pathological conditions of the ovum itself or to the conditions under which it was placed within the maternal passages. Thus it would lead us into the consideration of the monstrosities on the one hand, and intra-uterine amputations on the other.

The principal changes which affect the fœtus other than those mentioned above are changes dependent upon syphilis. These may show themselves in gummatous deposits in the internal organs, in various inflammatory alterations of the skin, in the production of that hepatic fibrosis to which attention has already been directed, or in the presence of specific inflammatory changes about the epiphysial cartilages of the long bones, and particularly the femur (syphilitic osteochondritis).

Amongst changes which may be rather regarded as accidental are those which consist in maceration and other alterations of the dead fœtus. In almost all cases in which the fœtus has died some little time before its expulsion from the uterus it is found to be softened and the skin to be peeling off. At the same time the meconium is found to have been expelled into the amniotic cavity. In other instances in which putrefaction has occurred the entire fœtus may be converted into a pulpy foul-smelling mass, the bones alone being recognisable, and even then the diaphyses of the long bones being separated from the epiphyses. In a few instances in which the fœtus has escaped into the abdominal cavity it remains localised without giving rise to any symptoms which call for surgical treatment, and then it may become impregnated with calcium salts and be converted into a '**lithopædion**.'

When the fœtus and membranes are expelled from the uterus entire earlier than the sixth month of intra-uterine life, the whole mass is called an **abortion**. When the abortion occurs towards the latter portion of this period the fœtus is already well developed, but when the abortion occurs during the first six weeks or two months the mass resembles a mere blood-clot unless especial pains are taken to determine its nature. This may be possible by discovering the fœtus or by determining the presence or absence of chorionic villi in the mass of clot if the fœtus has escaped. In many instances the future site of the placenta is recognisable, and it is very common to find that the tissues have become infiltrated with a considerable number of leucocytes, many of which may, by appropriate staining, be shown to be finely granular oxyphil cells.

SECTION XVIII

THE MAMMARY GLAND

Inasmuch as the breasts are, in reality, nothing more than specialised sebaceous glands, they ought, strictly speaking, to be considered along with the skin. Nevertheless, there are manifest advantages in describing the pathological processes to which they are liable in the present place.

(1) **Atrophy and hypertrophy.**—Atrophy of the mamma is characteristic of old age, and is a part not only of the general retrogressive changes which occur in old age, but also, in women, of the general decline of the sexual organs that occurs at the climacteric. The atrophy is not always obvious. In old women in particular, it is common to find that the glands are pendulous and apparently much enlarged. In most cases this enlargement is only apparent, and is due to the presence of an excessive amount of subcutaneous fat, the gland substance itself being either present in normal quantity or actually atrophied. Even in those cases in which the gland appears to be of normal size, it is generally found that there is a considerable increase in the amount of fibrous tissue and fat in the substance of the organ, and a corresponding diminution in the amount of true glandular tissue.

A similar atrophy occurs after lactation has ceased, whether this cessation takes place in the normal course of events when the infant is capable of taking solid food, or during the first few weeks after childbirth. In such cases the retrogression of the gland may pass beyond the normal, so that the ultimate result is a definite atrophy.

In addition to the above, atrophy of the mamma is found along with a large number of morbid processes, and then it is generally the result of pressure. Thus in cases of carcinoma or other new-growth of the organ, or in cases of inflammation which have been accompanied by the formation of an excessive amount of fibrous tissue, the gland undergoes a definite atrophy.

Hypertrophy of the gland is of less common occurrence, apart from pregnancy, but it nevertheless occurs. The breasts may be abnormally large in some individuals, as they are in most of the negroid races, but this is hardly the condition to which reference is made. The best example is given by those rare cases in which the male breast becomes enlarged until it resembles that of a female. Apart from a certain amount of discomfort, which may amount to actual pain, there is nothing more abnormal with the breast than its size. In the female the organ may become hypertrophied until it weighs twelve or fourteen pounds, but such a condition is very rare.

(2) **Inflammation (Mastitis).**—Inflammatory conditions of the breast are almost always clearly associated with functional activity, and although they may persist long after, they usually commence in the early days after parturition.

Acute mastitis is generally characterised by the appearance of one or more localised hard and extremely painful swellings in the depth of the breast. Over these the skin is stretched and shiny, and the amount of œdema may be great. A diffuse mastitis is rare. These swellings may undergo resolution, or they may proceed to the formation of abscesses, which point and burst and leave tortuous sinuses that open on the skin and lead down to the depth of the gland or down to the areolar tissue covering the great pectoral muscle.

The cause of the condition is almost always an infection from some small ulcer or abrasion on the nipple, and the infective agent is either staphylococcus or streptococcus. It extends from the surface by way of either the lymphatics or the galactophorous ducts.

Tuberculosis of the breast is a somewhat uncommon disease. It shows itself by the formation of cheesy nodules which break down and give rise to tortuous sinuses that may traverse the breast in all directions. From these sinuses there is discharged a thin pus, but the condition may become acute owing to the superaddition of ordinary suppurative processes. Occasionally the tuberculosis extends fairly widely before the pus finds an exit, and a so-called ‘ cold abscess ’ is produced.

Syphilis may affect the breast in the form of a primary sore, as when a wet-nurse is infected locally by an infected foster-child, or secondary manifestations may occur in the form of condylomata. In any case, it is rather the skin which is affected than the gland itself, for syphilitic mastitis and gumma of the breast are excessively rare.

In the case of **chronic mastitis** we are placed in the same difficulty that befalls us in the case of many other tissues; that is to say, it is uncertain how far the process is truly inflammatory. In chronic mastitis we find that the breast is harder than normal, and often smaller. The hardness is not generally diffuse, but is rather localised to the formation of one or more intensely hard foci, with definite connections to the mammary ducts. From these foci, however, the formation of fibrous tissue may proceed until the gland has largely been converted into a somewhat nodular mass of great hardness that raises the suspicion that the case is one of carcinoma. As a rule, the condition is present in both breasts, a point which serves to differentiate it largely from carcinoma.

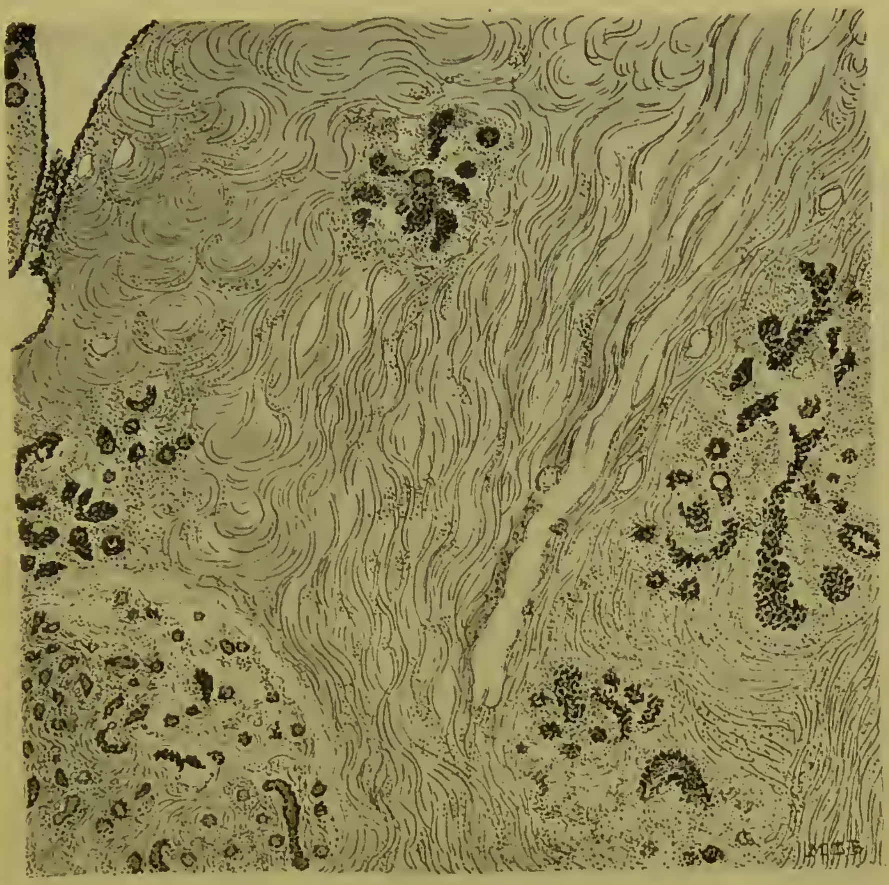


FIG. 151.—SECTION OF BREAST SHOWING CHRONIC MASTITIS. ×60.

The section shows extensive tracts of dense fibrous tissue with localised foci of compressed and atrophied mammary substance. At the left-hand upper corner a cyst is seen in section. In the immediate neighbourhood of the foci of mammary tissue a certain aggregation of leucocytes is observable.

If the condition is really inflammatory, it seems to start from the galactophorous ducts, and a condition is frequently met with in which there are definite thickenings along the course of certain of the ducts. Even here, however, there is practically no evidence that the primary condition is inflammatory, and it certainly does not tend to pass into any of the pathological sequels of inflammation.

A histological section of a breast which is the seat of chronic mastitis differs greatly from one of a normal organ. There is an enormous increase in the amount of fibrous tissue present, and the growth of this is accompanied by a pressure atrophy of a large part of the true mammary substance, as well as by a considerable alteration in the characters of that which remains. In the midst of the fibrous tissue are found foci of tissue which recall the acini of the gland, but differ therefrom in the facts that they have no definite arrangement, that the cells are smaller than normal though the nuclei stain well, and that the individual acini are greatly compressed. Hence it comes about that the cells themselves are pressed into contact with one another, and a condition is produced which very closely resembles certain forms of adenoma occurring in the breast. The resemblance is further increased by the fact that in places there occur a dilatation and an irregularity of the ducts which are affected by the compressing fibrous tissue. In some cases a definite proliferation of the cells of the acini takes place, so that collections of cells are produced ; in others there collects within the centre of the acinus or in the dilated duct a material which represents a secretion and which leads to the formation of a cyst. In the former instance it may be very difficult to distinguish the condition from that of a carcinoma. Indeed, many authors believe that carcinoma frequently commences in a breast which is the seat of chronic mastitis. Be this as it may, it is very common to find that a breast which is the seat of a carcinomatous nodule shows the presence of a chronic mastitis in the outlying regions.

(3) **New-growths.**—The breast is one of the commonest situations for the occurrence of both non-malignant and malignant new-growths, and it is general for these new-growths to be primary and not secondary.

With regard to the non-malignant growths, we may dismiss at once the fibroma, lipoma, and other simple growths of a similar kind with the remark that, though examples of most forms of neoplasm have been described as occurring in the breast, these varieties are excessively rare.

Adenoma.—The commonest non-malignant growth of the breast is the adenoma, with its sub-varieties, the fibro-adenoma and the adeno-cystoma. Adenomata pure and simple are somewhat uncommon, but they may constitute either the acinous or the tubular variety. The growths form circumscribed nodules that are generally of somewhat soft consistency. The acinous variety may be characteristic of the entire growth, but more commonly the greater portion shows the presence of the irregular clefts found in the ordinary fibro-adenoma, and acinous portions are few in number. The amount of fibrous tissue that is present varies considerably, as does its character. In some cases of fibro-adenoma, the density of the fibrous tissue is such that the mass would be regarded as a pure fibroma were it not for the presence of a small number of greatly compressed and irregular clefts that represent tubules of ducts. In other instances, the fibrous tissue, although present in considerable quantity, is so highly cellular that the growth may almost be regarded as a sarcoma. In yet other instances the cysts resulting from distension of the ductlike clefts constitute the most noticeable feature.

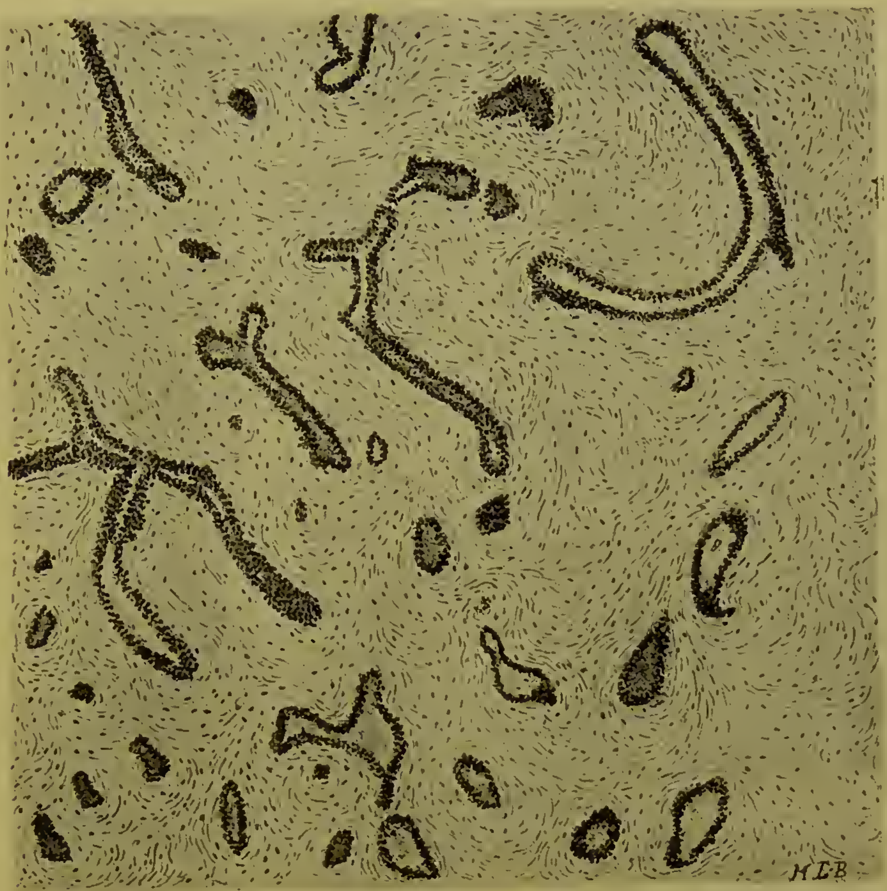


Fig. 152.—Section of Tubular Fibro-adenoma of Breast. × 70.

In a stroma of fairly dense connective tissue are situated numerous irregular clefts or ducts, some of which show in the lumen the presence of a small quantity of perverted secretion.

The epithelium lining the clefts and acini, in the case of the adenomata, is of the columnar variety, and is usually well formed. It is doubtful whether the clefts are lined by a single layer of epithelial cells. Although this would be best in accordance with preconceived ideas, particularly in the tubular adenoma, and although the view has been definitely adopted by some authors, it must be allowed that the actual appearances of microscopic sections favour the opinion that there is more than one layer of cells in the lining of the clefts. In the case of definite cysts the matter seems to be simpler, for it is not difficult, as a rule, to accept the view that one cell forms the whole thickness of the epithelial lining. The matter would be of comparatively little importance were it not for the relationship which appears to exist between the non-malignant adenomata on the one hand, and the malignant carcinomata on the other. There is a great deal of evidence that an adenoma may, in course of time, become carci-

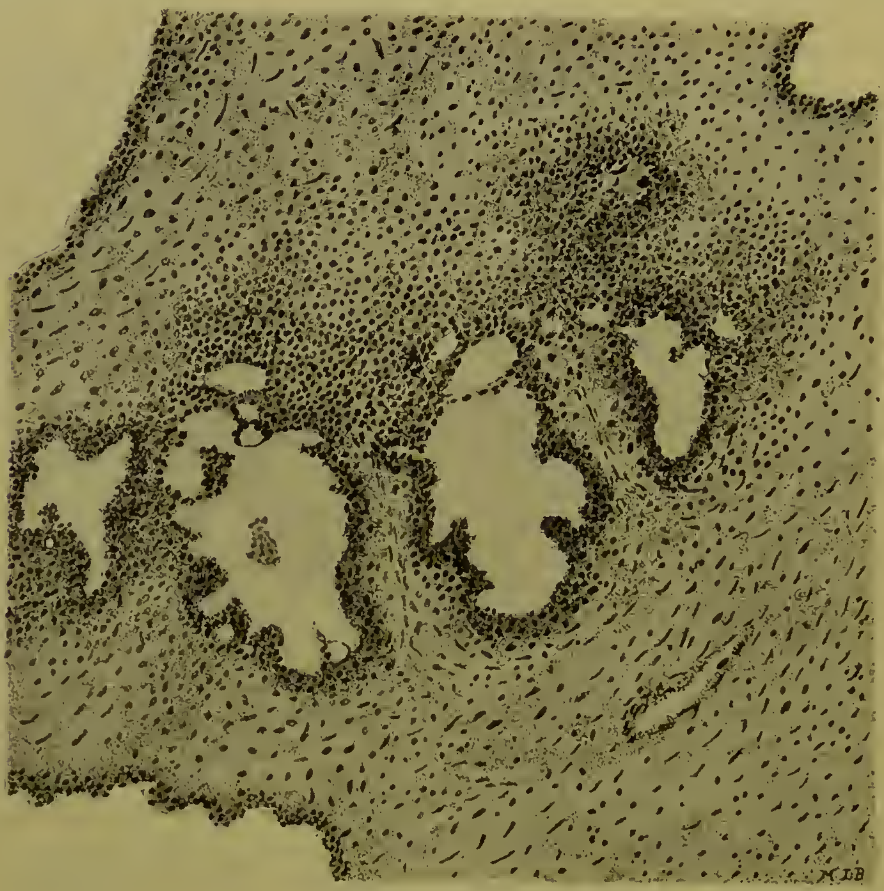


Fig. 153.—Section of Acinous Fibro-adenoma of Breast becoming Carcinomatous. × 420.

Portions of four acini are shown in which the lining epithelium has taken on a disorderly growth that is invading the connective-tissue stroma of the tumour. Portions of the walls of normal acini are seen at three corners of the figure.

nomatous. The method in which this comes about consists in the proliferation of the cells forming the epithelial lining of an acinus or a tubule, and an extension of the proliferating cells into the surrounding fibrous tissue (and subsequently into the substance of the breast itself) after the wall of the acinus or cleft has been broken through. A similar condition also occurs in the case of chronic mastitis—indeed, the appearances of a chronic mastitis becoming malignant, and a fibro-adenoma undergoing the same change, are hardly to be distinguished.

The adenomata and fibro-adenomata rarely form large masses in the breast, partly because of their slow growth, and partly because they generally come under treatment very shortly after they have been discovered by the patient. As a rule, they form nodules less in size than a walnut. They are usually somewhat nodular, and are contained in a definite capsule, from which they are to be shelled out with more or less ease. They are not fixed to the skin or deeper parts.

Carcinoma of the breast may show itself in the three varieties, spheroidal cell, columnar cell, and squamous cell, but of these the spheroidal-cell variety is infinitely the most common, and the squamous-cell variety infinitely the rarest. The spheroidal-cell carcinoma is found in two principal forms, either as an intensely hard growth (scirrhus) or as a soft (medullary) growth. Frequently the central portion of a mass of mammary cancer is hard and fibrotic, while the outlying portions are soft, and consist of alveoli filled with cells and separated by but little intervening fibrous tissue. At the extreme circumference of the growth, beyond the sensible limits, is an irregular zone of small round cells (leucocytes), amongst which are isolated epithelial cells of the carcinoma. (Figs. 55, 56, and 57.)

Columnar-cell carcinoma is found as the so-called 'duct carcinoma.' It is at times difficult to distinguish from the more cellular varieties of the spheroidal-cell carcinoma, owing to the tendency to the formation of intratubular growths which are closely pressed together. It has not, however, the same tendency to become scirrhoid in the centre as the spheroidal-cell growth. Moreover, it runs, clinically, a less malignant course.

The squamous-cell carcinoma is found to occur only on the surface of the breast, and then it is rather a carcinoma of the skin which is present in a somewhat unusual situation than a true carcinoma of the breast. Nevertheless it may involve the breast itself by its extension.

In cases of spheroidal or columnar carcinoma of the breast, whether the growth ultimately turns out to be highly cellular or not, the actual mass feels hard to the touch. It increases in size more rapidly if it is of the cellular kind, less rapidly if it is highly fibrotic, until at length it involves the skin and becomes attached thereto. Soon after this the skin ulcerates, and the growth, freed from restraining influences, grows rapidly and forms a fungating mass that breaks down on the surface and leads to the production of a foul ulcer. At the same time, particularly if the growth is of the spheroidal-cell type and occupies the outer and upper portion of the breast, small nodules of growth will be felt along the course of the lymphatics that run from the breast to the axillary lymphatic glands, and the glands themselves will be found to be enlarged.

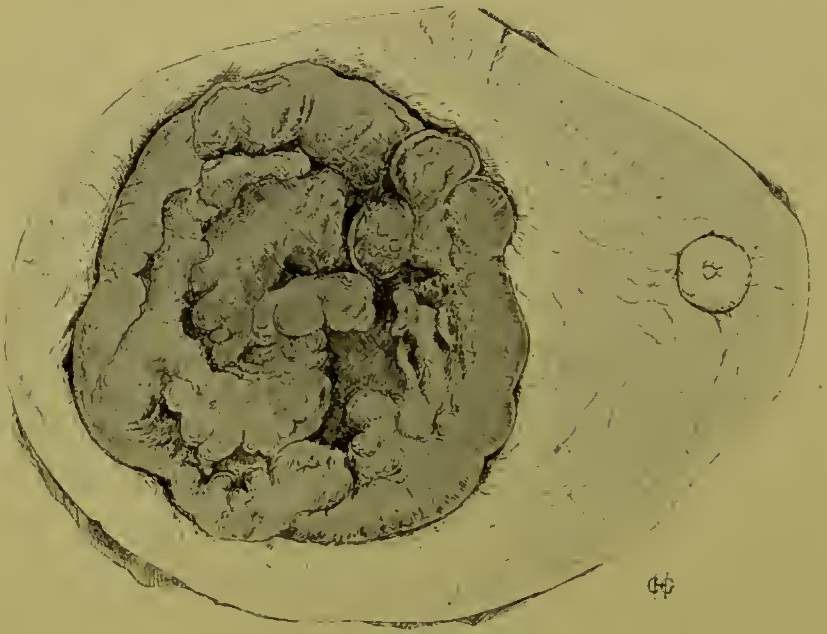


Fig. 154.—Fungating Malignant Ulcer of Breast. × $\frac{3}{4}$.

A considerable area of the skin has disappeared, and its place has been taken by a fungating mass, with deep crypts, that projects beyond the general level of the skin. The fungating mass was deep red and gave forth an intolerable stench.

When the growth lies close to the nipple, and therefore involves some of the galactophorous ducts, it tends to retract the nipple. Although this alteration is, in a sense, accidental, it is an important sign of the nature of the mammary growth.

In the case of the spheroidal-cell carcinoma the character of the growth varies somewhat according to circumstances. Thus, it may be so intensely hard that it grows very slowly and may even appear to diminish in size, or it may spread chiefly in the skin so that the skin of the breast and a large portion of the thoracic wall becomes converted into a material of the consistency of leather (cancer en cuirasse), or it may extend principally in the fibrous tissue lying between the gland itself and the great pectoral muscles, or it may implicate the pectoral muscles and thus fix the gland immovably to the thoracic wall.

After a primary mass of cancer has been removed surgically, secondary nodules are liable to occur along the track of the scar at some later time. These nodules are rarely of large size (if the prime operation was sufficiently extensive), they are multiple, and they do not show the same tendency to ulcerate. Moreover, a curious point with reference to them is that in some cases they have been known to disappear after they have definitely formed, and this in cases concerning the diagnosis of which there is not the slightest doubt.

Degenerative processes in the carcinomata other than atrophy and superficial molecular necrosis chiefly manifest themselves by the occurrence of the colloid change and the formation of cysts. The two latter changes are not very common, but sometimes one finds a case in which the name 'cysto-carcinoma' is merited.

In the case of the cystic carcinomata the cystic cavities may show the presence of numbers of intracystic growths of a papillomatous nature. These cases are probably somewhat special forms of columnar-cell carcinomata, for the papillomatous growths are covered by a layer of columnar cells. It has already been said that it is common, in the case of the duct carcinoma, to find that the dilated ducts are filled with densely packed papillomatous growths.

Sarcoma of the breast is very rare, but cases undoubtedly occur. In some of these there is no doubt of the diagnosis, for they consist of round or spindle cells which constitute the entire mass of the growth. But in other cases there is some difficulty in that there is present a large number of cysts which suggest that the growth is, in reality, a soft and rapidly growing fibro-adenoma. As a rule, in these cases we have to rely more upon macroscopic and upon clinical information than upon the microscope, and the view that the growth is malignant is upheld by the great size which it attains, by the rapidity of its growth, and by the way in which it tends to implicate the skin.

As a matter of fact, growths of the description just mentioned often raise the greatest difficulties from a purely histological point of view. For not only do they tend to be composed, so far as their stroma is concerned, of a large amount of highly cellular connective tissue which cannot be differentiated from spindle-cell sarcomatous tissue, but also the clefts and cysts which are present throughout the growths show a proliferation of their lining epithelium which raises the question as to whether they are not, after all, becoming carcinomatous. That is to say, these growths seem often to constitute a sort of intermediate class between the sarcomata and the carcinomata. By some authors the name 'sarcoma carcinomatodes' has been applied to them.

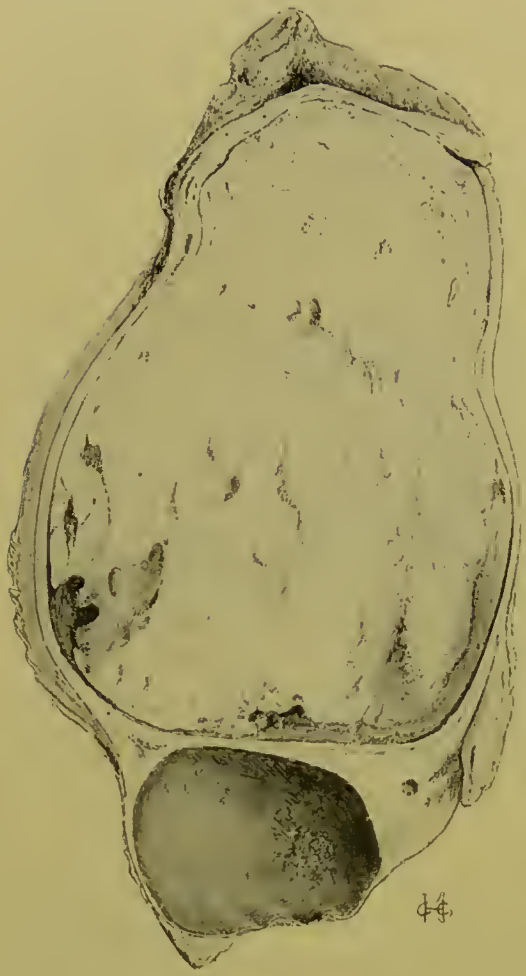


FIG. 155.—GALACTOCELE ('BUTTER-CYST'). × $\frac{3}{4}$.

Above is a large cyst of the breast filled with fatty material having the consistence of butter. Below is a smaller cyst which contained liquid somewhat resembling milk.

Cysts.—Mention has already been made, incidentally, of certain cystic formations, but cysts constitute so important a pathological condition of the breast that more than passing mention must be made of them.

Most of the simple cysts of the breast result from the distension of a galactophorous duct behind an obstruction. Thus we may meet with cysts containing altered milk in lactating women, or, if the cyst has been in existence for a considerable length of time, the contents may become converted into butter, or a fatty material which closely resembles butter. Such cysts are termed **galactoceles**, or, when the contents are semi-solid and fatty, **butter cysts**. They are of rare occurrence, and do not usually lead to any inflammation or other change in the surrounding glandular substance.

In other cases we meet with ramifying cysts in the breast that are filled so tensely with a clear fluid that it is supposed, before operation, that they are solid. These cysts are localised in one portion of the gland, and it is probable that they originate from dilated milk ducts.

Cysts not infrequently show the presence of papillary intracystic growths, though this is not ordinarily the case with galactoceles. These intracystic growths may be few or many, so that they may fill the cysts completely or may leave room for a considerable amount of cystic fluid. In the former instance the formation has close resemblances to the duct carcinomata. Owing to the fact that in some instances these papillomata are

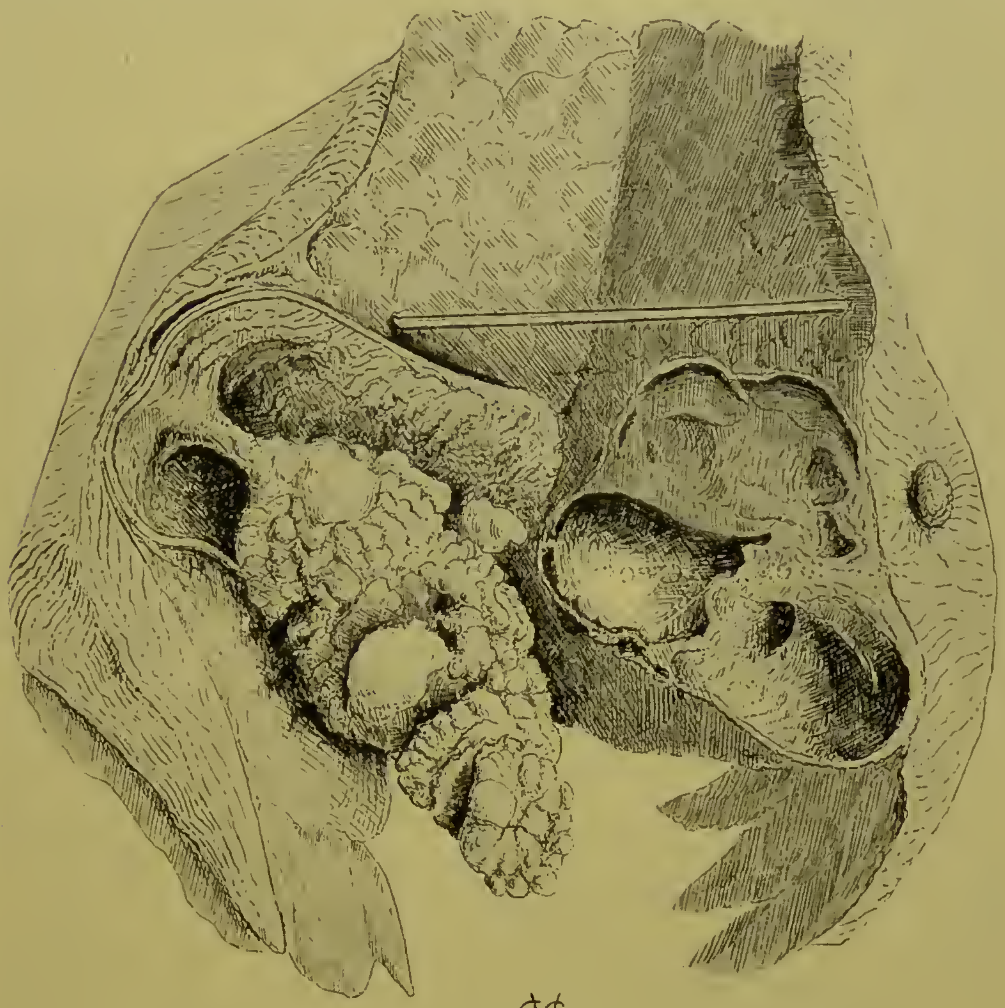


FIG. 156.—DUCT PAPILLOMA OF BREAST. NATURAL SIZE.

A cystic cavity has been opened and is seen to contain a large papillomatous growth which springs from the wall of the cyst and which, in the unopened condition, completely filled the cyst.

found to be present in cavities that are to be regarded with great probability as dilated ducts, the name of **duct papillomata** has been given to them. As to the exact relations between duct papillomata and duct carcinomata we are still in doubt.

Cysts which are present in adenomata and fibro-adenomata are also liable to show the presence of intracystic growths, but in these instances there is a smaller tendency for the growths to be greatly branched.

The **nipple** and the skin in its immediate neighbourhood are liable to be affected with certain inflammatory conditions, of which the commonest are those occurring during lactation, and associated with the formation of small, intensely painful, ulcers at the base of the nipple. In spite of their painfulness they are themselves unimportant, and heal without trouble when the special irritation is removed ; but they may be the seats of entry of those micro-organisms which lead to an acute mastitis, as has already been mentioned.

The nipple and the skin around is sometimes the seat of a disease of a somewhat special type. This disease has been named 'Paget's eczema,' after the surgeon who first called attention to it. It is in no wise a true eczema, but rather a destructive dermatitis of the papillary layer of the skin, which terminates in a somewhat peculiar form of carcinoma of the skin, and this again may terminate in a carcinoma of the glandular substance. The great distinction from true eczema, the existence of which is known, lies in the fact that, whereas eczema is amenable to the ordinary treatment for that disease, this is not the case with Paget's disease. Moreover, scrapings from tissue affected by Paget's disease show the presence of large vacuolated cells which are supposed by some to contain psorosperms, and this is not the case with true eczema.

SECTION XIX

THE SKIN AND ITS APPENDAGES

In this section only a cursory examination of the more common and important cutaneous changes will be made. For pathological changes in the skin, though differing clinically, do not offer so many variations as might be supposed from a histological point of view. Most of them, indeed, are but slight variations from the ordinary type of inflammation, and differ more in respect of the irritant which causes them than in respect of the actual inflammatory changes which are set up.

(1) **Atrophy and hypertrophy**.—Atrophy of the skin is one of the characteristics of old age, and shows itself by the wrinkled and pendulous appearances that are so well known. This change depends partly upon a general loss of elasticity, and partly upon a definite diminution in the thickness of the epidermis. At the same time the papillæ become shorter, and apparently many of them disappear altogether.

Similar changes to those met with in old age occur under all conditions in which the nutrition of the skin in general is greatly impaired. Thus, in cases of malignant disease or of chronic infective disease accompanied by great wasting, the skin of the body generally becomes dry, harsh, wrinkled, and inelastic.

Under certain conditions the atrophy of the skin is more pronounced. Attention has already been directed to the atrophy which results from pressure, but to that reference is not here made. The particular example in which this great atrophy of the skin is observed is that known as '**glossy skin**.' It occurs after, and seems to be a direct result of, interference with the nervous supply of the skin. Thus it is seen to affect the fingers after accidents in which the cutaneous nerves have been severed at the wrist or higher in the limb. The skin covering the affected fingers is intensely shiny and tense, so that it is impossible for the individual to properly flex the joints, if they are not actually rendered immovable. The skin itself shows a great thinness of the epidermal layers and an atrophy of the papillary layer of the true skin. At the same time the ordinary epidermal appendages —nails, sweat glands, &c.—are diminished in size and number, or disappear entirely. A similar, if not identical, alteration of the skin covering the fingers is often observed in the late stages of chronic rheumatoid arthritis.

So far as the cutaneous appendages themselves are concerned, atrophy is a somewhat common condition. In the case of the hair, atrophy of the hair sacs and the consequent falling out of the hair without a compensating subsequent reproduction of follicles is a characteristic of old age. The same, in some measure, is true of the various conditions in which the nutrition of the skin generally is greatly impaired, as after acute infective diseases, childbirth, and particularly in the early stages of syphilis. This atrophy of the hair follicles is not, however, always dependent upon these causes. Some persons become bald at an early age, and then it is probable that there is some congenital peculiarity with reference to the nutrition of the hair. In other cases the condition forms a definite disease (e.g. alopecia areata) with its

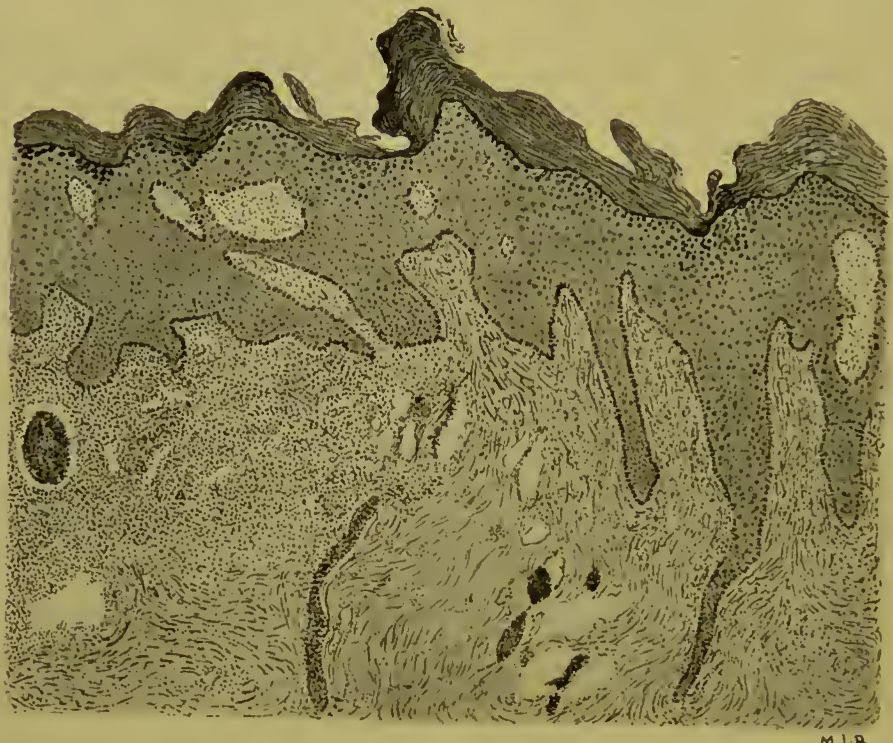


FIG. 157.—SECTION OF SKIN IN NEIGHBOURHOOD OF AN INFLAMMATORY FOCUS. × 60.

The left half of the corium shows the margin of the inflammatory focus densely infiltrated with leucocytes. The papillæ are irregular in shape, and inter-papillary processes of epidermis extend deep into the corium. The epidermal layers themselves are increased in thickness.

own characteristics. Here it is probable that the change is due to some vegetable parasite.

In other cases the nutrition of the hair fails, but the result is not so much a falling out of the hairs themselves as a brittleness, harshness, &c. This condition is closely analogous to the impaired nutrition of the nails which shows itself in the ridging and brittleness found in persons that have recently suffered from some severe illness.

Hypertrophy of the skin may affect the entire skin or only certain portions of it. Thus in the ordinary callosity we have a hyperplasia and hypertrophy of the epidermal layers not infrequently accompanied by an actual atrophy of the papillary layers. So, too, in the skin that borders upon an area of inflammation, the inter-papillary processes of epidermis are often enormously increased in length, passing downwards into the true skin for a considerable distance, and perhaps showing an irregularity that suggests the possibility that the condition is one of commencing squamous-cell carcinoma.[1]

This hypertrophy of the skin is really only dependent upon the presence in the part of an increased amount of nutriment. Thus it occurs particularly in the immediate neighbourhood of ulcers that have been in existence for a long time, and in cases in which there is some obstruction to the flow of lymph. It is frequently associated with an increase in the amount of hair formation, so that the presence of a large amount of hair is one of the most characteristic features in the neighbourhood of the chronic ulcers met with on the leg, or of the forearm or leg in cases of disease of the wrist or knee or ankle joints.

Overgrowth of hair is also found in the case of many of the congenital moles of the skin; and, apart from the presence of definite moles, it may be present over large tracts of the body. Under the latter condition it is generally termed '**hypertrichosis.**'

Overgrowth of the nails is a much less common condition. The best example of the condition in which it is seen is congenital heart disease, and then the nails may be more than double the ordinary size. At the same time they have the curved shape which is characteristic of the ends of the fingers in this form of disease.

In one condition the sebaceous glands seem to be the seat of an overgrowth. This occurs in **lipoma nasi**, in which the skin of the nose becomes hypertrophied and forms the bulbous end to the organ that is generally, but not invariably, seen in the case of elderly male drunkards. Microscopic examination of this tissue shows that it consists almost entirely of hypertrophied and hyperplastic sebaceous glands, the other elements of the skin showing little change except such as is dependent upon chronic inflammation. The condition, therefore, comes very close to the neoplasms.

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[1] It is important in this connection to note that care must be taken, when examining sections into the composition of which skin enters, that the section has been made at right angles to the free surface. Otherwise a number of these prolonged inter-papillary processes of epidermis may be cut, and give rise to the impression that the section has come from a squamous-cell carcinoma.

(2) **Pigmentations.**—Alterations in the amount and variety of cutaneous pigment will not call for prolonged remark, inasmuch as the whole subject of pigmentary degeneration has been dealt with fully in the first part. In some cases the pigment is present as a solid substance, in others a coloured solution permeates the cells. Cases in which the pigment is solid are afforded by argyria, tattooing, the melasma of Addison's disease, pigmentations due to sunburn, exposure to heat, and many others. Cases in which the pigment is in solution are most notably represented by jaundice.

Another class of case in which pigmentary changes of the skin occur is that in which there is a localised disappearance of a normal pigment. This is seen in **vitiligo** and **leucoderma**. The condition is sometimes known as **albinismus**. Microscopic examination simply shows a deficiency of the pigment normally present in the deeper layers of the epidermis and the most superficial layers of the dermis. In addition there will probably be found a certain degree of atrophy of the skin itself.

(3) **Vascular conditions of the skin not obviously inflammatory in nature.**—Some of the conditions that come into this class are certainly not of an inflammatory nature, but in the case of others the question is one which it is hard to determine. In the first category are œdema, congestion, hæmorrhage, gangrene, certain varieties of blister, &c. In the second are certain forms of erythema, purpura, urticaria, herpes, &c.

In **œdema** the macroscopic characters are an increased diameter of the skin and an infiltration of the subcutaneous connective tissue with the œdematous fluid. Sections of such skin are somewhat difficult to make, and in any case the tissue must not come under the influence of alcohol, otherwise the resulting picture will bear but little resemblance to the actual. The principal character of œdematous skin is the great degree to which the individual fibrils of fibrous tissue constituting the dermis are separated from one another. As a rule, there is found between them only a small amount of an indefinite granular substance, which is probably precipitated proteid from the slightly albuminous œdema fluid. The elements of the skin are swollen up, and have taken on a ground-glass appearance. Few leucocytes are present unless the œdematous skin has been the subject of a superadded inflammation. When the œdematous skin has been taken from the neighbourhood of a focus of inflammation, the microscopic section yields rather the appearances of a dermatitis than of a simple œdema.

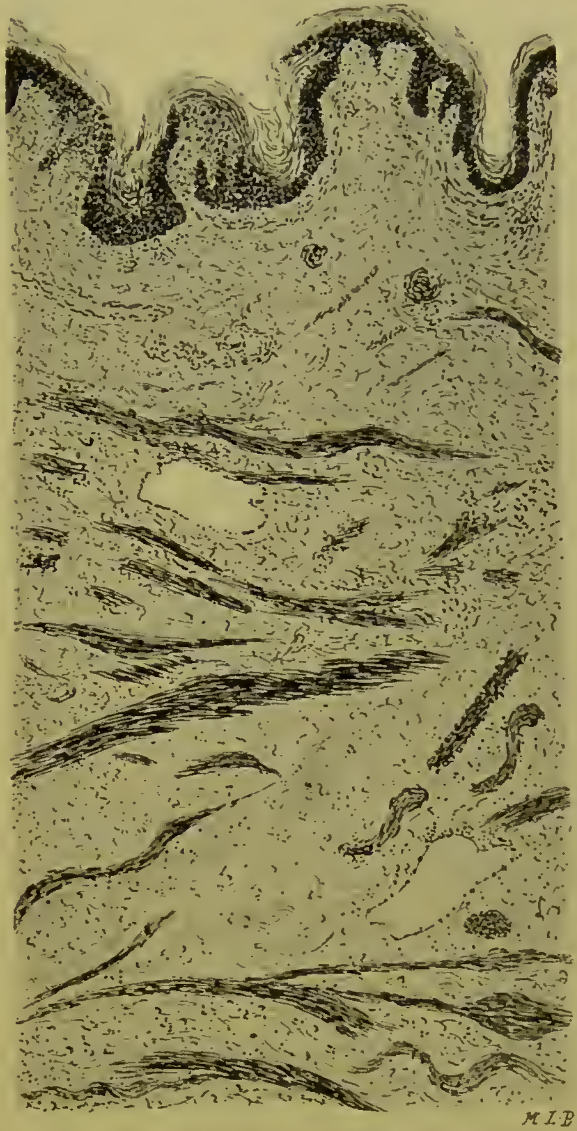

Fig. 158.—Section of Œdematous Skin (Scrotum). × 24.

The bundles of dartos muscle are widely separated from one another, and the connective tissue of the corium is very loose and broken up. Two lymphatics that are seen are widely dilated. Through the entire corium is distributed a granular material which has been represented by giving the figure a general grey tone. This granular material is proteid precipitated from the œdema fluid in preparing the section. The skin was hardened in 5 per cent. formalin, cut by the freezing method, stained in hæmalum, and mounted in Farrant's medium, in order to avoid dehydration by alcohol.

Congestion of the skin, when of the passive variety, is characterised, macroscopically, by the blue and swollen character of the part. In addition, if the venous congestion has existed for a long time, there is an increase in the amount of fibrous tissue present, so that the skin is not only altered in colour, but also in consistency. To other varieties of congestion sufficient notice has been given. In all cases the principal feature of congested skin in microscopic section is the presence in it of an abnormal number of blood-vessels that are abnormally full of blood. At the same time there may be evidences of pigmentation from the presence of blood-pigment derived from corpuscles that have been extruded from the congested blood-vessels.

Cutaneous **hæmorrhages** may show themselves in a variety of forms and may depend upon different causes. Amongst those which are not inflammatory, the most important are such as depend upon either alterations of the blood or alterations in the blood-vessels. Under one or both of these headings come the hæmorrhages that occur in **hæmophilia**. They may be minute, when they are generally termed **petechiæ**, or they may cover considerable extents of surface. Similar petechiæ are met with in cases of extreme anæmia not infrequently, and in the intense toxic forms of disease they are common. In the latter class of case they constitute **purpura**, but here, since it is not uncommon to find micro-organisms collected at the spots of hæmorrhage, it is probable that the condition is inflammatory, though of a very intense type.

Into the question of hæmorrhages that arise as the result of injury we need not enter. All that need be said is that the alterations in colour that the affected part undergoes depend upon alterations in the composition of the material situated in the tissues, and constituting different kinds of derived blood-pigment. This, of course, comes from the destruction of the extravasated blood corpuscles that have become situated in the tissues as the result of the injury itself.

(4) **Inflammatory affections of the skin.**—True inflammation of the skin constitutes the condition known as **dermatitis**, but although all inflammatory affections of the skin come under this designation in reality, it is commoner to restrict the name to the more or less acute condition in which the ordinary phenomena of inflammation are present. Thus the action of the sun's rays, or of heat in any other way, or of a large number of irritants, whether organised or unorganised, leads to an acute inflammation of the skin in which pain, swelling, redness, and heat are conspicuous. In a large number of cases special names are given to the conditions. Thus eczema, psoriasis, lupus, blisters, leprosy, and syphilis in their cutaneous manifestations, ulceration, &c., are all of them forms of dermatitis, though the actual appearances and the ætiological factors are so different.

Without attempting anything like a complete description of the different inflammatory appearances that may be met with in the skin, it is possible to indicate briefly the chief types of changes. These we may divide into the localised and the generalised, but it must be understood that a generalised condition is only one which is present over so large an area that it is convenient, rather than accurate, to separate it completely from the localised manifestations.

The *localised* manifestations are as follows :

(*a*) **Maculæ.**—Under this name are included all kinds of inflammatory staining of the skin which do not raise it above the general level of the surrounding surface. The staining may be brownish or red, and many of the minor forms of cutaneous affections come into the class. This, for example, is the case with erythema and many of the forms of the cutaneous rashes of secondary syphilis. In variola or small-pox, too, in addition to the characteristic pustular eruption, there is a macular eruption often present in the very early stages of the disease which shows itself principally about the lower part of the abdomen and the upper and inner parts of the thighs. The term is not applied to pigmentary stainings such as are found in vitiligo, Addison's disease, and such like.

(*β*) **Papules.**—A papule is raised and solid, and it is tacitly understood that it shall be of small size. The most characteristic papule is that found on the back in a simple case of measles. The papular is the commonest form of eruption, though it passes, in many cases, into either the vesicle or the pustule. Conversely, every vesicle or pustule was, at its inception, a papule. Histologically the papule shows merely a local infiltration of the more superficial layers of the dermis with leucocytes. No doubt a portion of the local enlargement is due to the presence of a greater amount of fluid than normal, and this can be proved by considering the large amount of fluid that escapes if a small puncture be made into the papule with a needle, but microscopic evidence of the fact is not given. Occasionally an extravasation of blood corpuscles takes place into the papule, and then the eruption is said to be **hæmorrhagic**. This may take place in the case of the eruption of measles, and is characteristic of the eruption of typhus fever. In some cases the papules contain micro-organisms. Thus the typhoid bacillus has been discovered in the characteristic 'rose spots' of that disease. When papules are present on a moist surface they are apt to attain to some considerable size and prominence.

(*γ*) **Vesicles.**—These are small elevated points which contain fluid. When pricked they collapse entirely, and as a rule their upper surface is convex. This is not invariably the case, however, for in varicella or chicken-pox the surface is umbilicated. The contents of a vesicle are clear fluid which contains a certain amount of albumin and therefore causes stiffening of any linen into which it may soak and subsequently dry. When a vesicle has existed for a certain length of time the contained fluid may become turbid or may dry up and form a scab in conjunction with the superficial layers of the epidermis. This is what happens in a large number of cases of eczema. In other cases, after the fluid has been discharged or absorbed the superjacent layers of epidermis may become detached in the form of scales, constituting **desquamation**. Desquamation varies considerably in respect of the size of the portions of skin that are detached. In measles, for example, the portions are so small that the desquamation is said to be 'branny;' in scarlatina, on the other hand, the portions of skin that fall off may be of considerable size; and in one form of eczema the desquamated portions may be several square inches in size and form practically 'gloves;' in the latter instance, however, it should be mentioned that the squames are not entirely composed of epidermis.

Somewhat specialised varieties of vesicles are formed by the conditions known as **sudamina** and **miliaria**. Sudamina are small watery vesicles found generally on the front of the thorax in persons who are the subjects of high fever. Their contents are quite clear, so that the vesicles are not easy to see except in certain lights. Their nature is somewhat doubtful, but it has been supposed that they are the result of blocking of the ducts of the sudoriparous glands—in other words, that they are of the nature of retention cysts. Miliaria are very similar in appearance to sudamina and arise under much the same conditions. They differ, however, in the facts that their contents soon become turbid and converted into a fluid resembling pus in respect of the number of cells which it contains, and that histologically there is an accumulation of leucocytes in the region of the openings of the sweat-glands.

(δ) **Pustules.**—The characteristic feature of the pustule is that it contains pus. Like the vesicle, it is generally bounded by a convex surface, but the surface, as in variola, may be umbilicated. Usually only one opening forms at the summit of the pustule, whereby exit is given to the pus. This is the case in the ordinary **boil** or **furuncle**. But when the mass of affected tissue beneath the raised epidermis is large, as in the **carbuncle**, several openings are formed through which the slough is discharged piecemeal. So far as the pustule itself is concerned, the central portion consists of nothing more than pus-cells together with a variable number of micro-organisms, which are probably either staphylococci or streptococci. But the tissues around a boil are always affected to a certain, and often to a considerable, extent. They are densely infiltrated with leucocytes and exuded fluid, and it is largely the presence of these two abnormal factors that accounts for the firm ring of tissue that surrounds a boil, and remains after the pus has been discharged.

The umbilication to which reference has been made, in connection with both the vesicle and the pustule, depends upon the fact that fibrous strands pass from the summit of the cavity to the deeper parts. These strands are filaments of the normal fibrous tissue of the dermis which have escaped destruction partly because of the general rapidity of the process, and partly because of the size of the area affected. In this instance the pus lies partly in the middle of the epidermal layers; but it also lies to some extent in the dermis, as is shown by the fact that scarring occurs as the natural method of repair in variola. In some instances the umbilication depends upon the fact that certain of the epidermal cells are liquefied, while others remain unliquefied. In this case the pustule, or more commonly the vesicle, does not necessarily affect the papillæ of the true skin, and recovery may take place without scarring. This, for example, is the natural course of events in varicella.

In **malignant pustule** (**anthrax**) the local manifestation of the *B. anthracis* is an intense hæmorrhagic inflammation with the formation of a black slough. Suppuration itself is quite a minor factor in the condition.

The *generalised* forms of inflammation of the skin belong, strictly speaking, to one or other of the conditions to which reference has been made above. Thus, simple erythema is in reality nothing more than a macula of exceptionally large extent; and urticaria or 'nettle rash' is an extensive and irregular condition which lies somewhere between the papule and the vesicle. That is to say, it is an inflammatory œdema of the skin. So, too, septic cellulitis is nothing more than a generalised form of pus formation, the actual inflammation showing itself by a diffuse formation of a thin and rapidly spreading pus in the subcutaneous cellular tissue. At the same time, the skin itself is affected and may undergo necrosis in large patches, or bullæ containing thin pus may be formed at various points at which the resistance to the pressure is least. A very good example of the relationship between the pustule and a condition of cellulitis is seen in the case of variola. For in the *discrete* form of the disease the pustules are separated from one another and have the ordinary characters of pustules with the addition of the umbilication, and in the *confluent* form the pustules are so closely placed that the entire surface of the part affected (generally the face) is covered by a continuous layer of pus held in position by the raised cuticle. In the confluent variety umbilication is lost.

In **erysipelas** we have a specialised inflammation of the skin which lies in a somewhat intermediate position. At the moment of its inception it is in undoubtedly a localised condition, and is then practically a papule. But the disease spreads with great rapidity in all directions until, finally, it comes to cover a considerable portion of the cutaneous surface. At the advancing edge the characters are usually those of an urticaria. The edge is raised and pale, and offers a marked contrast to the bright-red or reddish-purple part which constitutes the main portion of the inflammatory area. This advancing edge is rarely more than an eighth of an inch in width, and although it is generally present this is not invariable. The pale advancing edge is the situation in which the *Str. erysipelatis* is most likely to be found, and if sections are made of the skin it is seen that the micro-organisms fill the lymph spaces of the subcutaneous tissue.

The truly erysipelatous portion of the skin is red and swollen, but the affection tends to recede very soon after it has reached to its height, so that at the seat of origin the colour begins to fade after perhaps forty-eight hours, and returns gradually to the normal even while the affection is still spreading at the periphery. The recession of the disease is accompanied by a fine branny desquamation. As a rule, the inflammation in erysipelas does not go on to suppuration; but occasionally this occurs, and then bullæ are formed which contain a thin watery pus, or else a definite cellulitis is produced.

Special varieties of inflammation are also formed by the skin affections which are found in syphilis, leprosy, and tuberculosis, and other conditions in which the irritant is a specific micro-organism. Concerning the majority of these we shall not speak, but owing to the frequency with which lupus occurs a short account of the condition is necessary.

Lupus is in reality nothing more than a somewhat localised tuberculosis of the skin. At one time it was thought to be a disease *sui generis*, but it is now generally agreed that the micro-organisms found in the typical lesions of lupus are *B. tuberculosis.* The disease shows itself by the formation of a number of small hard, red, and raised papules, which in the course of a little time break down and leave an ulcerated surface. The papules are at first separated from one another, but by the formation of numbers of them the tiny ulcers become converted into one large ulcer. At the same time the originally discrete and papular nature of the disease is manifested by the presence of a number of small round, raised, reddish papules, which lie in the skin at a little distance from the definite edge of the ulcer. It is by the breaking down of these and their incorporation in the main ulcer that extension of the process takes place. The actual process, therefore, is exactly similar to that which constitutes tuberculosis in any other situation, such as the lung.

The macroscopic effect of the change is the production of an extensive ulcer with raised and everted edges and sinuous outline. One of the commonest situations for the disease is the face, and the destruction of tissue may be very considerable, leading, for example, to the destruction of a considerable portion of the nose and cheeks. The disease has some tendency to cicatrise at places in accordance with the more or less chronic character of tuberculous disease generally, but while it heals perhaps in the centre it continues to extend at the periphery. Dermatologists divide lupus into several varieties, but the pathological characters of all the varieties are fundamentally the same.

Histologically the characters of lupus are those of tuberculosis generally. Giant cells are of common occurrence, and with careful searching the tuberculosis bacillus may generally be found. The ulcerated portions of the disease show the presence of enormous numbers of migrated leucocytes, but pus, in the surgical sense of the term, is not produced in any quantity.

Before leaving the question of the inflammations to which the skin is liable mention must be made of certain conditions which are not themselves forms of inflammation, but which are closely allied with the subject in that they are the direct effects of irritants. Reference is made to burns, to bed-sores, and to perforating ulcers.

Burns are commonly divided into three classes, according to the degree to which the tissues have been affected. Thus, a burn of the **first** degree is one in which the skin has merely become reddened; a burn of the **second** degree is one in which the skin itself has become affected so that blisters are formed, and the epidermal structures are destroyed to a certain extent; while a burn of the **third** degree is one in which the effects of the heat have shown themselves by a charring of the deeper tissues, muscles, bones, &c.

Into the macroscopic and microscopic appearances of a part that has been burned it is not necessary to enter. The most important pathological features are those of the reaction that takes place in the still living tissues; and as these are nothing more than the phenomena of inflammation they do not call for discussion here. In the case of a burn of the first degree, if the patient survives no alteration of the tissues takes place; but if the burn has been of the second or the third degree, and recovery still takes place, the formation of cicatricial tissue frequently leads to great deformity owing to its contraction.

Although the subject of **blisters** might be considered along with the vesicle generally, there is some convenience in mentioning it here. Blisters are producible, of course, by many other agencies than heat, though heat is undoubtedly the most usual irritant at work. The blister is a collection of serous fluid beneath a raised portion of the epidermis, which may or may not contain blood corpuscles, but always contains a certain number of leucocytes. As a rule, the number of leucocytes is not great, so that blister fluid is usually quite clear. The variety of leucocyte found most commonly in blister fluid is the finely granular oxyphil cell. When the person in whom the blister occurs is already in an abnormal condition the characters of the blister fluid may also vary. Thus the fluid of a blister in a jaundiced person is deeply stained with bile pigments, and in a gouty person biurate of sodium may be found.

Bed-sores vary considerably in extent, but they all depend upon the fact that skin which is in a very low state of vitality is exposed to irritation. The irritant in many cases is merely pressure; in other cases the pressure is conjoined with imperfect cleanliness. The liability to the occurrence of bed-sores varies considerably. As a general rule, it may be said that if care be taken they are preventible; but nevertheless certain cases are found in which it is impossible to prevent the formation of bed-sores in spite of the most attentive nursing. This is particularly true when the central nervous system is at fault, as, for example, when there has been a fracture of the spine. The rapidity, too, with which a bed-sore appears varies greatly: in some cases it occurs only at the end of a long and debilitating illness, in others (and these are particularly cases of gross disease or injury to the central nervous system) they make their appearance within a few hours and spread with truly appalling rapidity.

Bed-sores are chiefly formed where there is pressure, and therefore over bony prominences such as the sacrum, the great trochanters, and the os calcis. They may first show themselves by the formation of a tiny red spot which rapidly passes into an abrasion, or a small bulla may form which takes on a similar course. In other cases a large area becomes rapidly black and gangrenous and sloughing takes place, exposing the bones and leading to their partial necrosis. Concerning the actual changes that take place in the tissues during the formation of a bed-sore it is unnecessary to speak, since they are identical with those which constitute gangrene generally. Since the conditions under which bed-sores occur are such as are accompanied by a profound interference with the general nutrition of the tissues, repair takes place so seldom that it is a pathological curiosity.

Perforating ulcers are really nothing more than specialised forms of the same condition as that which constitutes a bed-sore. That is to say, they occur only as the result of a trifling injury in a part which is insufficiently nourished. The actual cause of the deficient nutrition in the case of perforating ulcer is a sclerosis of the posterior columns of the spinal cord combined with alterations of the peripheral nerves. Hence the condition is very characteristic of **tabes dorsalis**. The condition usually commences in an insidious manner, and fails to attract much attention until the ulcer has perforated into the joint. The commonest situations for these ulcers are the toes, and their immediate origin frequently appears to be a slight injury, such, for example, as that received in the cutting of a corn. Histologically one finds evidences only of destruction ; signs of inflammation and repair are conspicuously absent.

(5) **New-growths.**—New-growths of the skin, as distinguished from the subcutaneous tissue, are not numerous, and practically confine themselves to the various kinds of epithelial tumours, non-malignant and malignant. New-growths starting in the subcutaneous tissue are, however, fairly common. Into a consideration of the greater number of these it will not be necessary to enter, inasmuch as they have been described in the earlier pages.

Amongst the non-malignant growths the commonest are the papilloma, the lipoma, the fibroma (generally seen in the pendulous form and constituting the condition known as **fibroma molluscum**), and the angeioma. Each of these has somewhat of a tendency to affect special parts of the body. Thus the papilloma is more commonly seen on the hands than elsewhere ; the lipoma in the fat-containing subcutaneous tissue of the loins and shoulders ; fibroma molluscum affects the skin of the trunk more particularly ; while angeiomata of the capillary and the venous type chiefly affect the face, and lymphangeiomata, which are much rarer, principally affect the limbs.

Among the malignant growths either sarcomata or carcinomata may be met with. The sarcoma may be either of the pigmented or the non-pigmented variety. In the latter instance spindle-cell sarcomata are the commonest, and this growth may occur in the form of multiple subcutaneous nodules scattered all over the body and showing but little tendency to break down. In the case of the pigmented (melanotic) sarcoma the primary growth is often very small, in spite of the fact that when the patient dies the internal organs, and particularly the liver, are found to be greatly involved by the secondary deposits. On the other hand, secondary deposits of melanotic sarcoma may take place in the skin itself. Thus large nodular and pigmented foci may be found in the subcutaneous tissue over a large part of the trunk. The carcinomata of the skin are of two kinds, either the typical squamous-cell carcinoma or the so-called rodent cancer. In both cases we find an invasion of the deeper tissues by an overgrowth of epithelial cells; but whereas in squamous-cell carcinoma cell-nests are almost always to be found, they are absent in rodent cancer. Moreover, as has already been said, it is doubtful whether the actual cells concerned are of exactly the same kind in both cases. At any rate, we find that alterations take place in connection with the sebaceous glands in rodent cancer which are not present in squamous-cell carcinoma.

SECTION XX

PATHOLOGICAL CONDITIONS OF THE EYE AND EAR

The pathological conditions of these two organs are so intimately bound up with their surgery that it is principally in surgical text-books that information upon their diseases must be sought for. Nevertheless a few words are necessary.

THE EYE

It will be convenient to consider separately the different portions which go to make up the entire organ, for the morbid changes that affect one part are different from those which affect another.

(1) **The conjunctiva.**—The commonest affection of the conjunctiva is inflammation, and it shows itself in a very characteristic form. For the redness, the pain, the heat, and the profuse secretion (which naturally takes the place largely of the swelling) are well known to every one. The irritant which leads to the inflammation is in the majority of cases mechanical, and then the inflammation is usually slight and transient. The fact that the conjunctiva is a mucous membrane is, however, well shown by the large amount of mucus which collects at the angles of the eyes and frequently causes the lids to be gummed together on waking in the morning.

In other cases the irritant is definitely bacterial, and then the catarrhal inflammation caused by the simple irritants, such as cold or a particle of dust, is replaced by a definite purulent inflammation. Any pyogenetic micro-organism may lead to the occurrence of a purulent conjunctivitis, but by far the most common is the gonococcus. This micro-organism, indeed, is accountable for almost all cases of blindness that date from childhood. Gonorrhœal conjunctivitis is not, however, confined to infancy, though it occurs far most commonly at that time of life owing to infection of the infant's eyes during parturition, but it is occasionally seen also in the adult. In these cases the infection has usually been directly carried from an infection of the generative organs. Unless the condition is treated vigorously it passes rapidly on to ulceration and necrosis of the cornea.

An infective form of conjunctivitis is that which is known as **granular conjunctivitis** or **trachoma**. It occurs frequently in Egypt and is not infrequently met with in schools in this country. It is characterised by a much greater chronicity than the forms which have previously been mentioned, and corresponding with this fact there is present a formation of minute masses of granulation-tissue. This granulation-tissue is chiefly composed of small round cells, and frequently it appears as if the mass of cells were surrounded by a capsule. The granules are very often found on the conjunctival surface of the eyelids, and by the irritation which they occasion a marked conjunctivitis is kept up, the cause of which is not discovered until the lids are everted. The little masses of tissue frequently rupture and lead to the formation of minute ulcers, which irritate the cornea and set up ulceration. These ulcers of the cornea are very characteristic in appearance, for the cornea being an avascular part it is necessary for the blood-vessels concerned in the inflammation to pass from the circumference of the cornea to the seat of the ulcer. This they generally do only on one side, so that a narrow band of intensely congested minute vessels is seen to be tracking across one side of the cornea. Such a condition is known as **pannus**. If granular conjunctivitis persists for a long time, the conjunctiva becomes altered by the formation of a large amount of cicatricial tissue. This dense tissue may lead to the disappearance of the granules on the eyelids, but it is a potent cause of a continuance of the inflammation.

Diphtheria and tuberculosis affect the conjunctiva only with great rarity, but it is common for persons with a tuberculous history to suffer from a subacute form of inflammation of the conjunctiva at the margins of the lids. This condition is characterised by congested eyelids, marked interference with the development of the lashes, and the presence of a small amount of dried secretion with which the lashes are almost always clogged to a less or greater extent.

(2) **The cornea.**—We have already referred to one of the most important affections to which the cornea is liable—viz. ulceration.

This condition may extend until the entire cornea has sloughed, when the aqueous humour escapes and there follows a complete disorganisation of the eye. In other cases the weakening of the cornea, associated with the presence of a large amount of aqueous, is followed by a protrusion of the cornea (**staphyloma**). In yet other cases the corneal ulcer heals with the formation of an opaque cicatricial mass which interferes to a greater or less extent with vision. Frequently, however, in all these conditions the inflammation extends to the iris, and then it may be adherent to the cornea, with the certainty that other severe changes will supervene later.

Inflammation of the cornea (**keratitis**) may be of the kind which has been described above, but it is perhaps commoner to reserve the term 'keratitis' for that interstitial form which is hardly ever seen except in the shape of a cloudiness of the normally transparent tissue. The condition is undoubtedly met with most commonly in persons who are the subjects of hereditary syphilis, and occurs in conjunction with other signs of the disease. It is uncertain how far the condition is met with in the absence of syphilis.

The cornea is also liable to be affected in certain nervous conditions, although these are not of common occurrence. Thus, in herpes occurring along the course of the orbital branch of the fifth nerve, and in paralysis of the fifth nerve itself, the cornea may become affected. In all cases of this kind the ultimate result is the same, and consists in the formation of a corneal ulcer.

(3) **The iris, ciliary body, and choroid.**—When the entire globe of the eye is affected, all these parts naturally take part in the disease, but considered separately it is commoner for the iris to be the seat of disease than either of the other parts.

Iritis occurs most commonly as the result of syphilitic inflammation, whether of the acquired or of the hereditary variety, but it is also seen along with rheumatism and as the result of injury. The inflammation is generally acute, but the degree of inflammation varies considerably in different cases. In the mildest forms there is an output of a considerable amount of fluid (serous iritis), and this may pass off without the production of important changes. But far more commonly the inflammation is of the fibrinous type, and then the fibrin becomes deposited upon the edges of the iris and attaches it to the posterior surface of the cornea. In this way an impassable obstruction is presented to the escape of the aqueous humour which accumulates within the anterior chamber. A far more important result lies in the fact that the fibrinous adhesions between the iris and the cornea (**synechiæ**) are constantly lighting up the inflammation afresh, so that unless their formation is prevented there is a great fear that the usefulness of the eye will become permanently impaired, even if the repeated attacks of intra-ocular inflammation do not disorganise the eye itself so considerably as to call for its removal for fear that the inflammation will spread to the other eye.

Inflammation of the ciliary body (**cyclitis**) is liable to occur in connection with inflammation of either the cornea or the iris. The effects of the inflammation are to be seen in alterations in the characters of the intra-ocular fluids, for the part is intensely vascular, and it probably plays the principal part in the formation and regulation of the vitreous and aqueous humours. **Glaucoma** is believed to depend upon the alteration of the relations between the iris and the ciliary body. It consists in an increase of the intra-ocular tension, and this may depend either upon an increase in the amount of fluid poured out into the chambers of the eye, or upon a deficient absorption from them. The condition is but little understood, so far as its pathology is concerned, and it would not be profitable for us to delay in order to consider it here.

The principal change which is undergone by the choroid is an alteration in its pigment. In some cases this appears to be the result of inflammation (frequently syphilitic), but in others, although the ophthalmoscope reveals marked changes, no explanation of them can be given. It is necessary to bear in mind that the choroid is one of the situations from which a melanotic sarcoma may originate.

Other changes affecting the parts under consideration do not call for particular remark, with the exception of tuberculosis. Tubercles are sometimes found on the iris, and in cases of generalised tuberculosis, whether they are accompanied by pronounced meningeal symptoms or not, minute miliary tubercles are often present, although they are not always easy to discover. The tubercles themselves are of the ordinary kind, and do not appear to undergo any marked subsequent changes.

(4) **The lens.**—In childhood the lens is very soft, but as years go on the central portion becomes dense, although it does not lose any of its transparency. The lens itself is contained within a capsule lined by an epithelium.

The only morbid change that we need consider is **cataract**. This condition depends almost always upon an alteration of the character of the outer laminæ of the lens, in the course of which they become infiltrated with globules of fat. At times this cortical portion becomes converted into a fluid substance, in which are suspended fat-globules, crystals of cholesterin, and general detritus.

Although a cortical cataract is by far the commonest form, a variety is known which depends upon a fatty alteration of the epithelial cells of the capsule of the lens. This constitutes the **capsular** cataract. The fatty change of the epithelial cells is generally preceded by a marked proliferation.

The chief condition which determines the occurrence of cataract is old age, but it may also occur as the result of injury or in the course of diabetes. It is questionable whether in the case of the last-mentioned disease the cataract is not the product of the senile changes which so frequently accompany diabetes, rather than a direct result of the diabetic condition itself.

(5) **The retina and optic nerve.**—The retina is the subject of several important morbid changes. Thus it may be in whole or in part detached, or it may become altered owing to the occurrence in it of hæmorrhages, or again it may be the seat of a definite inflammation.

In detachment of the retina a mass of material, either blood or serous fluid which undergoes partial coagulation, lies between the retina itself and the back of the eye. The condition is often the result of injury, but it sometimes occurs without appreciable cause. As a rule, too, the amount of retina which is detached is so considerable that the utility of the organ is markedly impaired, if it be not entirely destroyed.

Retinal hæmorrhages are of a different kind from that hæmorrhage which leads to detachment of the retina. They are said to be 'flame-shaped,' from their appearance. The extravasated blood lies along the course of the blood-vessels from which it has escaped. These are almost always arterioles running over the surface of the retina. The condition occurs chiefly in chronic fibrosis of the kidney, a disease in which the arterial pressure is greatly increased at the same time as the arterial walls are altered. But flame-shaped hæmorrhages are also sometimes met with in renal disease of the acute type, and occasionally under conditions in which there is an extreme anæmia. Thus, in leuchæmia, retinal hæmorrhages of considerable size may occur at the latter end of the disease and lead to complete blindness. As a rule, although the hæmorrhages in question undoubtedly impair the sight, they do not lead to complete blindness. The reason of this is that they are often most conspicuous in the periphery of the retina.

The retina is sometimes the subject of definite inflammation, but the condition which is known as **retinitis** is usually the result of the inflammation rather than the inflammation itself. The entrance of the optic nerve, however, is frequently the seat of inflammatory changes, and then we get a condition of neuro-retinitis to which reference will be made shortly.

In the change which is generally known as retinitis the principal appearance is that of a pigmentary alteration. Hence the condition is known as **retinitis pigmentosa**. It is characterised by the presence of irregular patches of dark and light over the whole retinal field. The reason of the change largely lies in the fact that the choroid shares in the inflammation. The patches of pigment generally lie along the course of the vessels.

The principal acute changes which occur in the optic nerve are those which depend upon either an increase in the amount of fluid in the sheath of the optic nerve, or a direct extension of an intracranial inflammation to the sheath of the optic nerve and subsequently to the nerve-fibrils themselves. These changes are summed up in the conditions known as **optic neuritis** and **choked disc**.

In **optic neuritis** we find that the edges of the optic disc are blurred instead of being sharply defined, as is normally the case. The blurring passes for a short distance over the retina and constitutes **neuro-retinitis**. At the same time, the disc, instead of being somewhat depressed below the ordinary level of the fundus of the eye, is raised irregularly, the alteration being due to the local accumulation of a large number of leucocytes and the presence of an excessive amount of inflammatory exudation fluid. The blood-vessels passing through the optic disc become compressed by the exudation fluid, and are less easily visible for this cause, and also because they are hidden somewhat by the accumulated inflammatory products. As a consequence, they undergo changes, and in their turn induce changes in the tissue of the retina in their immediate neighbourhood. They become the centres of lines of opacity which radiate irregularly over the retina, particularly in its fibrous layers. Apparently many of these streaks undergo subsequently a fatty degeneration, but some of them are white from the first. If the condition which causes the neuro-retinitis is primarily renal, or if a renal element enters into the case, a certain number of hæmorrhages may be present also, and some of these may subsequently undergo changes which lead to white appearances indistinguishable from those which are frankly inflammatory from the first.

The microscopic alterations in neuro-retinitis are very variable, but the chief variations depend upon the amount of fluid and the number of extravasated leucocytes concerned in the changes. In some cases the sheath of the nerve is crowded with leucocytes, many of which have found their way in between the fibrils of the nerve itself. This may be easily seen if longitudinal sections are made. In these cases a section through the lamina cribrosa shows that the connective tissue is greatly thickened, that the number of cells present is large, and that the nerve-fibrils are obviously compressed. In other cases, in which the changes are principally œdematous, there is a scanty number of cells, though a larger number is present than normal, but the fibrils of the nerve, especially where they pass through the lamina cribrosa, are obviously compressed and are surrounded by an enlarged clear space which, during life, was filled with inflammatory fluid.

In the condition known as **choked disc** we really have nothing more than the appearances which depend upon a localised venous congestion of the eye. That is to say, the prime cause of the altered appearance of the disc is an accumulation of fluid within the sheath of the nerve which prevents the free passage of blood from the interior of the eye by way of the optic venules. It follows that the condition is characterised by a swelling of the disc and an engorgement of the venules. Subsequently there may supervene a definite inflammation, so that the condition passes into one but little differing from optic neuritis.

The ultimate end of an optic neuritis and of a choked disc is a fibrosis or sclerosis of the nerve-fibrils, with an atrophy of the proper nervous elements. Hence the conditions are very likely to terminate in optic atrophy and permanent blindness.

In **optic atrophy** we have an alteration of the optic nerve and particularly the entrance of that nerve into the eye, which is characterised by an abnormal whiteness of the optic disc, a diminution of its size, and a comparative absence of the vessels which normally enter at its centre and course thence over the retina. The condition is one of sclerosis, and sections show the presence of an abnormal amount of dense fibrous tissue in all those places in which fibrous tissue is normally present (particularly in the lamina cribrosa), as well as a complete, or almost complete, absence of nerve-fibrils. The condition may be subsequent to neuritis or to choked disc, as has already been said, or it may supervene gradually as a process of sclerosis identical with that which occurs in the spinal cord itself. The latter variety of change, indeed, is particularly liable to occur in connection with the sclerosis of the posterior columns of the cord which constitutes the chief alteration in tabes dorsalis. Optic atrophy, it will readily be understood, is accompanied by a gradually increasing impairment of sight, and when the atrophy is complete the blindness is also complete and permanent.

In connection with the optic nerve and the retina it must be mentioned that the central artery of the retina, which enters the eye in the centre of the optic nerve, is sometimes occluded by an embolus. The effect of such an occlusion is, of course, immediate blindness, and subsequent changes occur in the eye which are characteristic of embolism. The accident is especially likely to occur in cases of organic disease of the heart, but it is rarely seen. The cptic vein may also become blocked by thrombosis.

(6) **The globe as a whole.**—Before leaving the eye it is necessary to mention certain conditions which affect the eye as a whole. The most important of these is **sympathetic ophthalmia.** This condition consists in an intense inflammation which takes place in one eye at some time after its fellow has been the seat of a panophthalmitis, induced generally by some injury. It is very difficult to explain the exact way in which the changes in the second eye are produced. In the greater number of cases it is probable that the irritant is bacterial, and travels along the optic nerve on the affected side as far as the chiasma, and thence down the opposite nerve. But in some cases it is possible that the inflammation is of a reflex nature, in the sense that it is dependent upon nervous causes. The condition is very likely to occur if an injury has been received by one eye which involves the vitreous and therefore the ciliary body.

Tumours of the eyeball.—The two most important as well as the commonest new-growths of the eye are sarcoma and glioma. Sarcoma is either of the spindle-cell variety or else alveolar, and in any case it is generally pigmented and springs from the choroid. The growth extends very rapidly and involves the whole globe; but even if the globe be removed the disease reappears within a short time in the orbit, and destroys life, partly by its extension to the brain, and partly by reason of the secondary growths which appear in distant parts. The condition appears sometimes to have a tendency to occur in successive generations. Glioma is far less commonly seen than sarcoma. It springs from the retina, and usually increases rapidly in size.

The tumour has the ordinary histological characters of a glioma, and consists of a number of cells with numerous branching and interlacing processes, a small amount of cell protoplasm, and a relatively large nucleus. It is not uncommon for the number of cells to be sufficiently great for the growth to merit the name of a glio-sarcoma. Under these circumstances the sarcomatous character dominates the entire clinical history of the case.

Non-malignant tumours of the eye, and carcinoma, are so rare that they do not call for especial notice here. The same is true of the animal parasites, although *Cysticercus cellulosæ*, the hydatid form of *Tænia solium*, and the common form of the hydatid of *Tænia echinococcus* are occasionally met with.

THE EAR

In connection with the ear we have to consider the auricle, the external auditory meatus, the middle ear, and the internal ear.

(1) **The auricle.**—The affections of the auricle are principally those of the skin generally. Thus it is often the seat of eczema, and it may be affected with carcinoma, of the ordinary squamous variety, or with rodent cancer. So, too, small fibromata may form on the lobule as the result of the irritation of earrings.

The most independent affections of the auricle are, however, **tophi** and **hæmatomata**. Tophi are small accumulations of sodium biurate which occur in gouty persons, and are identical in composition, and, though much smaller, in appearance, with the chalk-stones that form on the knuckles in gout. Hæmatoma consists in an extravasation of blood between the cartilage of the ear and the perichondrium. It is occasioned by injury, but the injury is usually very slight, or the condition may appear to arise spontaneously. It occurs chiefly in insane persons, and particularly in those who are suffering from **general paralysis**. For this reason the condition is sometimes spoken of as **insane ear**.

Various minor malformations of the auricle are of common occurrence. One of the most interesting is that in which there is a small tubercle on the anterior part of the tragus which corresponds to the operculum of fishes.

(2) **The external auditory meatus.**—This part of the ear is the seat of many affections, the great majority of which are of minor importance. Eczema, furuncles, erysipelas, accumulations

of cerumen, fungi, papillomata, polypi consisting of granulation-tissue, are the commonest. All of these are apt to lead to an inflammation of the meatus which, owing to the swelling of the parts and the accumulation of inflammatory material, induces partial or complete obstruction of the canal. If the condition has existed for a long time, the inflammation may pass to the bony canal, and then the ordinary changes characteristic of osteitis, whether rarefying or sclerosing, are produced.

The external auditory meatus is bounded internally by the tympanic membrane, affections of which are very common. It may be affected either from within or from without, but in either case it is probable that the disease will be represented by a perforation of the membrane. These perforations may be small, when they not infrequently heal, or they may involve the whole or the greater part of the membrane. In the latter case repair is out of the question. It is commoner for alterations of the tympanic membrane to depend upon disease of the middle than upon disease of the external ear.

(3) **The middle ear.**—Of all diseases of the auditory apparatus, that affecting the middle ear is by far the most important, by reason of the intimate connection which it has with the brain on the one hand and the mastoid cells on the other. In fact, it may be said without fear of contradiction that, when disease of the middle ear is present, the question as to whether the patient will or will not suffer an impairment of hearing is a matter of quite subordinate importance.

The middle ear is an air-containing cavity of very complicated form. The middle portion lies immediately behind the tympanic membrane, and through it passes the chain of auditory ossicles. From its lower and anterior portion passes the Eustachian tube, which opens in the naso-pharynx, and from the upper and posterior part there is a communication with the mastoid cells. The mastoid cells are for the most part small, but one cell—the antrum—is large, particularly in childhood. The upper boundary of the antrum mastoideum and of the tympanic cavity is a thin plate of bone which is the sole separation from the cranial cavity. In the young even this thin partition may be deficient in places. The entire middle ear is lined by a very delicate mucous membrane.

The principal disease to which the middle ear is liable is inflammation. This inflammation may be acute or chronic, and may be followed by unimportant results or by a complete disorganisation of the part. One mild form of inflammation is that which practically constitutes nothing more than a catarrh; it may supervene in the course of an ordinary coryza, and then the inflammation extends to the ear from the throat by way of the Eustachian tube. Frequently, too, it remains principally localised in the tube itself. The result of the condition is an impairment of hearing from the general swelling of the mucous membrane, and possibly a perforation of the tympanic membrane to allow of the escape of the retained mucus, &c. As a rule, the trouble is only temporary. If the condition persists, the mucous membrane becomes stiff and rigid, and local adhesions may be formed. The result of this is often a permanent impairment of the pliability of the tympanic membrane, the ossicles, and the membrane closing the fenestra rotunda. Calcification, too, and local formation of new bone may further complicate the condition. The deafness consequent upon these changes is likely to be susceptible of but little improvement.

Acute suppurative inflammation of the middle ear (**otitis media**) is one of the most important complications of scarlet fever, and, more rarely, of other exanthemata. Apparently the condition arises owing to an extension of the pharyngeal inflammation. In other cases the pneumococcus is found in the pus which escapes from the middle ear, and must be regarded as the cause of the inflammation. The inflammation always goes on to perforation of the tympanic membrane; in fact, the middle ear is converted into a sort of abscess cavity. The internal and external ears may share in the inflammation, but this is not very common.

After an acute suppurative inflammation has been in existence for some little time the acuteness subsides, and a condition is left which constitutes **otorrhœa**, and in which there is a permanent escape of a watery and perhaps offensive discharge from the ear. The explanation of this condition is that, owing to the loss of the tympanic membrane, the mucous membrane of the middle ear is exposed to the action of numberless irritants, and these, co-operating with the pyogenetic cocci that fail to be properly removed, practically convert the middle ear into a discharging sinus. This sero-purulent condition persists at least until the contents of the tympanic cavity, and particularly the ossicles, have been discharged, and by that time the mucous membrane of the middle ear has been converted into a granulation-tissue which completely fills up the tympanic cavity and may, in its turn, lead to the formation of polypi, to caries of the bone, to abscess of the brain, to suppurative meningitis, to septic thrombosis of the lateral sinus, or to general pyæmia.

The mucous polypi to which reference has been made above are of the same type as those which are formed elsewhere. They consist of prolongations of the inflamed and œdematous mucous membrane, and frequently the central parts become cystic. Occasionally they reach to a considerable size, and protrude through the annulus tympanicus into the external ear. It is unnecessary to say that they play a considerable part in keeping up the inflammation.

In spite of the formidable results which may supervene upon otitis media, it is important to note that they do not tend to occur so long as a free exit is given to the discharge, and, as a corollary, so long as the discharge does not become offensive. In cases of cerebral mischief dependent upon antecedent ear disease, a history is almost always given of an otorrhœa which, after persisting for some time, had recently ceased.

The changes in bone which may occur in connection with middle-ear disease are of the ordinary kind. As a rule, the osteitis is rarefactive, and sequestra may be formed which are subsequently exfoliated. Thus, in the Museum of St. George's Hospital there is a beautiful specimen of the entire bony semicircular canals and cochlea which were removed in such a case. More commonly the dead bone is removed in small portions only. In addition to this variety of osteitis, a sclerosis of bone may occur, and then the resulting bone is of ivory hardness. This change is particularly likely to occur in connection with the bony walls of the mastoid cells.

(4) **The internal ear.**—Morbid conditions of the internal ear are rarely primary, except so far as they concern the auditory nerve itself, and, in connection with this tissue, macroscopic and microscopic changes are so little known that the majority of the diseases, distressing though they are to the patients who suffer from them, are of the 'functional' class. Nevertheless the internal ear may be affected secondarily in cases of disease of the middle ear. One of the most important affections of the internal ear which is probably primary is that which constitutes **Menière's disease,** a peculiar form of giddiness and loss of sense of equilibrium. This sense is, as is well known, intimately bound up with a normal condition of the semicircular canals, and though it cannot be said that all cases of Menière's disease depend upon obvious changes in the semicircular canals, and perhaps in some cases these parts are not to be inculpated at all, there is no doubt that sometimes they are the seat of hæmorrhage.

In all cases in which the labyrinth has been interfered with, deafness results, and may be permanent. When this occurs in childhood, deaf-mutism supervenes. Deaf-mutism, however, is not solely dependent upon labyrinthine disease, for any morbid condition of the auditory apparatus which is bilateral and leads to pronounced deafness before the child has learned to speak well is followed by the same result.

SECTION XXI

THE NERVOUS SYSTEM

THE diseases of the nervous system are so various, and the system itself consists of so many parts, that it will be necessary to consider the subject under several different headings. In spite of this, however, it must be remembered that in many diseases more than one part of the entire system is affected, while, in some, every part of the nervous tissue suffers, though in different degrees in different places.

I. THE BRAIN AND ITS MEMBRANES

It will hardly be necessary to distinguish between the cerebrum and the cerebellum, but the diseases which affect the cerebral membranes are in so many points different from those which affect the brain substance itself, that it is necessary to deal with these separately.

(1) The Cerebral Membranes

Although the brain is surrounded by dura mater, pia mater, and arachnoid, it is not necessary to consider these separately. For when one of them becomes the seat of disease it is impossible for the others to escape entirely. Nevertheless it may be said that the chief affections of the meninges are those in which the more delicate membranes are involved, and for this reason the general term 'leptomeningitis' has been given to them. This name also implies tacitly that inflammation is the commonest affection of the meninges.

Leptomeningitis may be either acute, subacute, or chronic. The appearances which are found in definitely acute and in definitely chronic cases are quite different, but in the subacute cases, although there is no doubt that clinically they are different from either of the two other varieties, the appearances approximate closely to the acute type.

It is doubtful whether a *simple* meningitis occurs apart from the results of traumatism in which there has been no fracture of bone. Such cases are excessively rare, and the chances of examining brains which have been subjected to traumatism that has not led to fracture, but has nevertheless been followed by death at a sufficiently short interval after the injury, are equally rare. We do undoubtedly find, however, cases in which there is a localised thickening of the meninges that might easily be the result of a simple meningitis. This thickening is similar to that which is seen in the case of the capsules of the spleen and liver and in the so-called 'corns' of the heart, and calls for no further remark. In the acute stage we practically never meet with simple meningitis.

Of the forms of meningitis that are definitely dependent upon the action of micro-organisms, three stand forth prominently. These are the suppurative, the tuberculous, and that which, from the particular position which it affects, is known as the posterior basic. Each of these calls for a somewhat detailed description.

Suppurative meningitis.—When the meninges are the seat of suppuration the degree to which they are affected varies very considerably. In some cases there is only a slight inflammation, which causes adhesion of the cortical substance of the brain to the membranes, and of these, in their turn, to the bone of the skull. Here the amount of suppuration is very small, although the entire condition may be called forth by an intensely suppurative condition, such as that which, starting from a purulent otitis media, culminates in the formation of a definite abscess within the brain substance itself. On the other hand, we meet with cases in which the entire surface of the brain is bathed in a thick layer of creamy pus. This condition again may originate in disease of the middle ear, but it may also originate in disease of the nose or the orbit; and in some cases there does not appear to have been any primary focus of suppuration upon which the meningeal suppuration can be regarded as being secondary. The cases of the last-mentioned kind are generally very severe, and the amount of pus present is large. Their explanation is very doubtful, but it can be said with certainty that in a large majority of them it is possible to demonstrate the presence of the pneumococcus both by cover-slip preparations and by culture.

Apart from differences such as have been mentioned above, all cases of suppurative meningitis show a general resemblance.

Thus, we always find that the pus is present in largest quantity in the sulci between the convolutions, that it lies beneath the pia mater, that it shows a general tendency to gravitate to the base of the brain, and particularly to fill up the lozenge-shaped space at the base formed by the optic chiasma and the crura, and to track along the course of the blood-vessels in the Sylvian fissures.

The macroscopic diagnosis of suppurative meningitis is not always quite easy to make. For the general yellowish appearance characteristic of pus is offered by that fibrinous material which is formed in many varieties of meningitis which are not suppurative. In these latter cases the number of 'pus cells' present is extremely small, whereas in truly suppurative meningitis the material present beneath the membranes is pus in the strict sense of the term.

The bacteria that are present in the pus are either staphylococci, streptococci, or diplococci. In the case of the staphylococci and streptococci there is no difficulty, but when we meet with diplococci there is always a necessity to determine whether these are pneumococci or a variety of micro-organism known as *Diplococcus meningitidis intracellularis*. The importance of the latter micro-organism lies in the fact that it is specially associated with certain forms of meningitis. To these attention will now be turned for a short time.

Cerebro-spinal meningitis.—This disease may show itself either in an epidemic or in a sporadic form, the former being commonest in Germany, the latter in this country. In either case we find that the entire brain and cord is covered by a thicker or thinner layer of pus. When the pus is present in large quantity it distends the membranes of the cord in particular. In other cases of cerebro-spinal meningitis the amount of pus is so small that it may be almost said to be non-existent. The clinical course of the disease is then much more chronic, so that the variety of disease almost comes into the class of chronic meningitis. There is reason to believe, however, that the cause, or causes, of the conditions are the same in all cases. In a large number of them it is proved that the *Diplococcus meningitidis intracellularis* is present, and there is great reason to believe that it is the actual cause of the disease. It is not quite certain, however, that this micro-organism is the sole cause of cerebro-spinal meningitis. The contrary is probably far nearer the truth. For cases have been recorded in which the pneumococcus and not the intracellular diplococcus has been present.

Posterior basic meningitis.—While we are dealing with this point it will be well to mention another variety of meningitis concerning which a similar diversity of opinion exists so far as its ætiology is concerned. Reference is made to posterior basic meningitis, a disease which affects children almost solely, and which is also more commonly found to affect females. The disease in question is generally seen in a chronic form; indeed, the extreme chronicity is one of the most important points in its differentiation from other inflammatory affections of the meninges. Nevertheless it is sometimes met with in an acute form, and then the duration of the disease is to be reckoned by days instead of by months, as is the usual case.

Whether acute or chronic, posterior basic meningitis shows much the same post-mortem appearances. Such differences as obtain will be noted in passing. It differs principally from the other varieties of meningitis which we have considered in the fact that the amount of inflammatory exudation is always small, and in some cases so small that it is difficult to believe that the clinical symptoms can have been fully dependent upon the conditions that are actually found. The macroscopic changes consist essentially in the presence of a small amount of gelatinous material present in the lozenge-shaped space at the base of the brain. This is generally present in largest quantity at the posterior part of the brain, and from this circumstance the disease has derived its name. When a case is very severe it may be found that a small amount of inflammatory material is present along the course of the vessels in the Sylvian fissures, but it is quite characteristic of the disease that there is a complete absence of any inflammatory material over the convexity of the brain, and almost as characteristic that the inflammatory exudation does not extend for any distance down the cord. In the most acute cases this is practically the only change which is present; but in the commoner and more chronic cases it is usual to find that there is a certain amount of inflammatory material over the upper surface of the cerebellum which has occluded the foramen of Magendie, and has led in this and in other ways to an interference in the passage of the cerebro-spinal fluid from the cavities of the brain to the subarachnoid space, and therefore has caused an accumulation in the ventricles. The effect of this accumulation is seen in two directions. In the first place, the ventricles themselves are greatly distended; and in the second place, the convolutions become much flattened owing to the unyielding nature of the skull. There consequently is brought about a certain degree of **hydrocephalus**. To accommodate this increased amount of intra-cerebral fluid, the fontanelles and sutures of the cranium separate somewhat, and the size of the head is increased. The degree of hydrocephalus in cases of posterior basic meningitis is rarely considerable, but whenever the case has been at all chronic it is always unmistakable.

The character of the exudation in posterior basic meningitis varies somewhat, but it always differs essentially from that in the suppurative forms of meningitis in that it is never pus. It must be granted that in some cases the amount of fibrin present is so considerable that it gives to the fluid an appearance which, without the aid of the microscope, might easily be mistaken for pus, and it was to cases of this description that reference was made earlier. In other cases—and these form, perhaps, the majority—the intra-ventricular fluid is clear and almost colourless, while at the base of the brain, when the organ has been removed, it is difficult to believe that there has been present that gelatinous-looking material which is clearly recognisable when the frontal lobes are pulled backwards at the autopsy to facilitate the division of the cranial nerves and the cord below the bulb. Even in cases in which this clear fluid is the only alteration obvious at the first glance, it may be found that there is present a certain amount of definite fibrin on the ependyma of the ventricles, and particularly over the choroid plexuses, but sometimes it is quite impossible to discover any solid material whatever.

The question as to the ætiology of cases of posterior basic meningitis is in practically the same state as that concerning the ætiology of cerebro-spinal meningitis. Indeed, some authors maintain that posterior basic meningitis is merely a sporadic form of the ordinary cerebro-spinal meningitis. Be that as it may, there is no doubt that, so far as the bacterial side of the ætiology is concerned, a large number of cases of posterior basic meningitis are associated with the presence of the Diplococcus intracellularis, while some undoubted cases of the disease are as certainly dependent upon the action of the pneumococcus.

In dealing with posterior basic meningitis we have already overstepped the boundary-line between the acute forms of meningitis and the chronic. As, however, we have only to describe one other variety of chronic meningitis, we shall mention this here, and shall then return to the consideration of the tuberculous variety, which is undoubtedly acute.

In chronic meningitis, as the term is generally understood, we have to do with a universal thickening of the meninges, and particularly the pia mater. Not only is this membrane thicker than normal—it is also much more opaque. Hence there is less difficulty in distinguishing cases of chronic meningitis after death than might be supposed. Such a thickening of the meninges is one of the commonest changes found in the brains of those who have died in lunatic asylums.

Tuberculous meningitis.—Of all the varieties of meningitis, that which depends upon the presence of tubercles in the membranes is the most important, not only by reason of its actual severity, but also by reason of its frequency. Although it is far commoner for children to be affected by tuberculous meningitis than adults, persons of full age—even of middle or advanced age—are sometimes affected.

In all cases tuberculous meningitis is but a special manifestation of a generalised miliary tuberculosis. As a rule, the primary focus from which the generalisation has taken place is the lungs, although in children it is perhaps more common for the prime focus to have been in the bronchial glands, one of which has softened and broken into a pulmonary vein. In a very few cases the prime focus has been a caseous tuberculous nodule in the brain itself, but far more commonly such foci lead to death from pressure, &c., without the intervention of a meningitis. When, in children, the primary focus has been in a bronchial gland, the tuberculous process may have spread into the lung before the softened gland has broken into the pulmonary venule, and then we have the appearance of a definite pulmonary tuberculosis from which it may appear that the generalised infection has taken place. In any case, it is common for the lungs to show a larger number of tubercles than any other part, although the actual death has been due to the presence of the smaller number within the cranium, associated as they are with the presence of a considerable amount of fluid exudation and fibrin.

The seat of the miliary tubercles in tuberculous meningitis is almost always the walls of the small blood-vessels, and particularly the middle cerebral artery and its branches. It is therefore in the Sylvian fissures that we must look for the principal evidences of the changes induced by the tubercles—viz. the fibrinous exudation. With care, too, it may be possible to distinguish definite miliary tubercles with caseous centres upon the walls of the arterioles. They are best seen if the vessels are removed from the surface of the brain and are floated out in water. But even if they are not actually seen as small irregular protuberances upon the walls of the vessels, those walls are themselves altered. The chief change consists in the presence of a lowly organised granulation-tissue which greatly increases the thickness of the arterial wall.

In common with other forms of meningitis, it is usual to find in tuberculous meningitis that the principal accumulation of inflammatory exudation is in the lozenge-shaped space at the base of the brain. This space is generally filled with a gelatinous mass, which may have the translucent appearance found in posterior basic meningitis, but is commonly more opaque, and therefore has a greater resemblance to pus. The number of cells, however, in the exudation is small, and the exudation in no wise merits the name of pus. From the above-mentioned region the inflammatory material tracks along the Sylvian fissures up towards the convexity of the brain. In some instances the convexity itself is largely covered by the fibrinous material, but as a rule this is not the case. Nevertheless it is common to find small patches of fibrin ('lymph') at various points over the convexity beneath the pia mater, and situated in the sulci left between adjacent convolutions.

Another situation in which it is very common to find some evidences of the inflammation is over the dorsal surface of the cerebellum, close to the foramen of Magendie. It is in part owing to the closure of this foramen that there occur an accumulation of fluid in the ventricles and a flattening of the convolutions themselves. The flattening in cases of tuberculous meningitis is generally considerable, but the actual amount of imprisoned fluid is usually not great. From this it follows that the enlargement of the ventricles of the brain, though present, is not of great extent. The fluid within the ventricles is usually of a slightly turbid nature, but the turbidity is due rather to the presence of small particles of fibrin than to the presence of cells. Small numbers of migrated leucocytes, principally those of the non-granular type, are, however, present.

In the miliary tubercles on the blood-vessels the specific bacillus of tuberculosis may sometimes be found. The search for them is almost always a prolonged one, and unfortunately it is often fruitless.

In adults the changes present in the meninges in cases of tuberculous meningitis are almost always far more conspicuous than they are in children. And this, although the symptoms of the intracranial condition are much more marked in the young. Indeed, in adults it may have been quite unsuspected during life that a condition existed which is laid bare at the autopsy.

It is frequently said that a very common situation for the miliary tubercles in cases of tuberculous meningitis is the choroid plexus on either side. It is true that it is common to find small accumulations of fibrin in this situation, but it is doubtful whether the tubercles are more apt to affect this situation than any other. As a matter of fact, it is unsafe to assert that a given mass is a tubercle unless it has been subjected to microscopic examination.

When the substance of the brain is cut into in cases of tuberculous meningitis it is found that it is of softer consistency than normal, and that the outer layer of grey matter is distinctly thinner than usual. These changes are obviously due to the distension that the accumulation of fluid in the ventricles has occasioned and the saturation of the solid material by the pent-up fluid.

Glanders.—Localised accumulations of caseous or curdy material may be found on either side of the dura mater in this disease.

(2) MORBID CONDITIONS OF THE MENINGEAL VEINS AND THE VENOUS SINUSES

Before leaving the consideration of the morbid conditions of the meninges it is necessary to devote a small space to those conditions which definitely depend upon alterations in the circulatory apparatus. Of the arteries, the middle meningeal artery is of especial importance. The veins constitute the cerebral sinuses that run between the layers of the dura mater and the veins of the pia mater. Of the sinuses, the most important from a pathological point of view is the lateral.

Circulatory disturbances arising in the meninges are essentially of two kinds. In the case of the arteries the trouble consists in the outpouring of a quantity of blood which accumulates beneath the dura mater, and between it and the brain, and gives rise to symptoms of compression; and in the case of the venous sinuses the most important pathological condition is thrombosis, which generally arises in connection with some inflammatory condition of the bone in the neighbourhood.

Meningeal hæmorrhages are often of considerable size, and the amount of compression which the brain may undergo as a result of the hæmorrhage is well seen if a transverse section of the skull with the contained brain is made, and the degree to which the falx has been displaced is noticed. Meningeal hæmorrhage is very frequently seen in cases that have died from severe accident which has involved the head, but has not been accompanied by considerable fracture of bone. It may happen, however, that the fracture is found at the autopsy to be of far greater extent than was originally supposed. This is particularly likely to be the case in fracture of the base.

In some cases it appears that such hæmorrhages can occur and, for a time, be recovered from. That is to say, in insane persons it is not very uncommon to find a yellowish-white mass having much the consistency of wash-leather, and lying in close apposition to the inner surface of the dura mater. Such masses are usually bilateral. For a long time they were the subject of much speculation, but it is now generally agreed that they are the representatives of former hæmorrhages. The masses are also generally laminated, and it is supposed that the blood from which they were formed was poured out in successive quantities. They are composed almost entirely of fibrin, but in that part which is nearest to the dura mater there is often a definite formation of new fibrous tissue. A condition essentially similar to that which has just been described is sometimes found in infants that have been born with the aid of forceps through a greatly flattened pelvis. In these cases, however, the mass consists definitely of coagulated blood, unless the child grows to some years. In addition to the fact that it will most probably be of very deficient intellect, when it dies a bilateral thickening of the dura mater will be found presenting the appearances that have been described. The condition is sometimes known as **pachymeningitis hæmorrhagica.**

When the venous sinuses are affected the only change of importance is thrombosis, but the subsequent changes which may be undergone by the thrombus, and the changes which may secondarily be induced by the thrombosis, are of the utmost importance.

Thrombosis of the sinuses occurs in two totally different classes of individual. In the one class we have to do with persons of advanced old age in whom the circulation is very feeble. In the members of this class the thrombosis is generally extensive, and it may practically involve the whole system of sinuses running in the dura mater. A similar condition may, of course, be met with under any set of circumstances in which the action of the heart is very feeble. Thus it occurs sometimes in insane persons at quite an early age. In all cases of this extensive description the meningeal veins are thrombosed to a greater or less extent as well as the sinuses themselves. Somewhat more rarely a more or less general thrombosis of the meningeal veins, with or without extensive thrombosis of the sinuses themselves, occurs in cases of embolism of a principal branch of the cerebral circulation, such as one internal carotid or one middle cerebral artery.

In the other class of case we have generally to do with a young adult who has been for some time the subject of otitis media or some kindred disease of the ear, or some disease of the nose. In these cases the disease may spread directly by way of the petrous portion of the temporal bone to the inferior petrosal sinus and thence to the lateral sinus, or it may extend by way of the mastoid cells or the frontal sinuses to the nearest venous sinus. In any case, the nearest sinus becomes blocked by a thrombus; and since the inflammation which has led to the thrombosis is infective and generally suppurative, there is a great likelihood of the coagulum in the venous sinus being infected in its turn. As a result, it softens, and portions are carried into the general circulation, setting up a general pyæmic condition.

Embolism of the cerebral arteries, although it ought, from one point of view, to be considered along with the meninges, is so intimately bound up with changes in the brain substance itself, that we shall defer reference to it for the present.

II. THE BRAIN

(1) **Retrogressive changes**—(*a*) **Red and white softening.**—Of the degenerative processes affecting nerve-matter, the most important is softening. This is of two kinds—red and white; but, although there is a macroscopic difference between the two varieties, the essential difference consists in nothing more than that in the red variety there is an admixture of red blood corpuscles which is absent from the white variety. The conditions, too, under which red and white softening occur are identical.

Softening depends upon an interference with the nutrition of the affected part, owing to which it dies and undergoes that liquefaction which is characteristic of all soft tissues when they die. The cause of the local death is in most instances a cerebral embolism, and then the focus of softening is more or less strictly localised to the area supplied by the occluded artery. But thrombosis of veins will also lead to the change if the number of obstructed veins be sufficient to completely deprive a certain portion of the brain of nutriment. The situations of the softened areas, and to a large extent the appearances, are different in the two cases. For with embolism it is more common for a central portion of brain substance to be altered, whereas when the veins are thrombosed over a large area there is a liability to the occurrence of a more or less extensive area of softening that is superficial, and therefore chiefly concerns the grey matter. So, too, in a central softening we almost always find that the softened mass is devoid of blood corpuscles or of hæmatogenous pigment, whereas in cases of venous softening the altered cortical substance shows the presence of a large number of red corpuscles, both normal and in various stages of disintegration.

In the case of a focus of white softening it is generally impossible to determine the fact except by the altered consistency of the affected part. The altered consistency is, however, usually so evident that the nature of the case is recognised at once. Thus, in a case in which the softening has gone on to an advanced point the affected area may almost present the appearances of an abscess. On the other hand, if death has occurred very soon after the occlusion of the vessel and death of the part involved, it is extremely difficult to be certain on the point. When softening has definitely commenced, the microscope generally reveals its existence partly by alterations in the medullary sheaths of the nerves, which show evidences of breaking up, and partly in the existence of large leucocytes filled with fat-globules (' Gluge's corpuscles '), which are always present wherever there is a disintegration of nervous material. At the same time it is possible to see a number of loose fat-globules of various sizes, together with remnants of neuroglia. When the softening has proceeded further, no remnant of nervous tissue is recognisable, but there is a uniform creamy material which contains no cells other than the large Gluge's corpuscles already mentioned, a number of fat-drops, and a granular *débris*. It is probable that under favourable circumstances these softened foci may become removed, just as an infarcted area may be removed elsewhere in the body. This may, perhaps, account for some of the cysts containing a slightly coloured watery fluid that are met with from time to time in the brains of aged persons. It must be conceded, however, that a considerable percentage of these cysts have resulted from former hæmorrhages into the brain substance. To them we shall refer later.

It is not necessary to enter into a full description of the appearances met with in red softening, for they differ only from those of white softening in respect of the blood corpuscles and blood pigment which is present. In severe cases the amount of blood present is so considerable that the brain substance is the seat of numerous punctiform hæmorrhages. As the hæmoglobin readily diffuses from the extravasated corpuscles into the surrounding softened substance, the whole mass takes on a colour that varies (according to the actual constitution of the altered blood pigment present) from a deep red or purple to a yellowish green. It is hardly necessary to add that the latter colour is rather characteristic of small foci of softening, the former of areas so large that their formation has been incompatible with a continuance of life.

From what has been said above it is clear that softening is essentially nothing more than a fatty degeneration taking place in a dead tissue.

(β) **Pigmentation.**—Pigmentary changes in the case of the brain are of two kinds. In the one the pigment is hæmatogenous, and the general explanation of the presence of the pigment is that there has been, at some time not too close to the patient's death, a cerebral hæmorrhage, whether spontaneous or traumatic. The most important point in connection with the pigment present is that it may occur in either of two forms—hæmosiderin or hæmatoidin, the latter of which is remarkable in that it contains no iron and is practically identical with bilirubin. It is also considered that its formation is carried out without the intervention of living cells, whereas this is not the case when hæmosiderin is produced. As a rule, such pigment is only found in very small quantity, and then it is usual to find a small cyst in the substance of the brain with pale yellow watery contents, and a wall which is indistinguishable from the brain substance, into which it gradually merges, except for the fact that that part which is closest to the cavity of the cyst is of a rusty red or orange-yellow colour. Under the microscope the characteristic crystals of hæmatoidin are readily recognisable.

The other form of pigmentation is non-hæmatogenous and affects the nerve cells themselves. The significance of the pigment is uncertain beyond the fact that it is present in greater amount as the individual advances in years. After about the age of forty a certain amount is always present. It is found more especially in the large multipolar cells, and a favourite situation is around the nucleus in the large motor cells of the ventral cornua of the cord (fig. 9). The pigment stains an intense black in cords treated by Marchi's method, from which it may perhaps be surmised that the granules composing it are of a fatty nature. But upon this point one cannot be dogmatic. One thing, however, is certain, and it is that they do not consist of fat pure and simple.

(γ) **Atrophy and hypertrophy.**—Upon these conditions it is not necessary to speak at length. There is no doubt that the weight of the brain decreases with advancing years, and that in the aged the organ appears shrunken and allows of the presence of a larger amount of subarachnoid fluid than is normal in the individual of middle age. So, too, it is certain that persons of greatly deficient intellect, and those who die in lunatic asylums, often have brains below the normal weight. But it is equally certain that mere weightiness of brain is not an evidence of superior intelligence. For the largest brain on record, which is in the Museum of St. Bartholomew's Hospital and weighs seventy ounces, was obtained from the body of a young boy of somewhat below the ordinary degree of intelligence. And numerous records are extant that place this point beyond doubt.

So far as the microscopic changes are concerned which are present in atrophy and hypertrophy of the brain, they are extremely meagre. In hypertrophy, in fact, it is impossible to discover any histological change whatever, and in atrophy there is only present a certain amount of shrinkage of the cells, combined with the fact that they lie in larger lymphatic spaces than normal.

One of the most important varieties of atrophy of the brain is that which is due to pressure and is associated with the presence of an excessive amount of cerebrospinal fluid in widely dilated cerebral ventricles (**hydrocephalus**). As to the cause of hydrocephalus it is impossible to speak with anything that even approximates to certainty. We feel confident that there must be some interference with the escape of the fluid within the ventricles, but as to the actual character of the obstruction, and even more as to the cause upon which the existence of the obstruction itself depends, we are completely ignorant.

Hydrocephalus itself is easily recognisable, even during life. For the great distension of the ventricles with fluid leads to a corresponding enlargement of the head; and as the condition obtains almost entirely in young rickety children in whom the anterior and posterior fontanelles have not properly closed, the distension is more marked than it would be if it occurred in an adult. Moreover, it is easy to feel that the fontanelles themselves are widely open, and to see that the general shape of the cranium is altered.

In a marked case of hydrocephalus the brain substance is converted into a mere thin layer in which the differentiation between grey and white matter is hardly to be made out. This layer is placed in close apposition to the meninges, and although evidences of the convolutions are present the sulci between them are extremely shallow. The anatomical arrangements of the interior of the brain are equally disturbed, and, in particular, the basal ganglia are apt to be thinned out until they are hardly distinguishable as such.

The condition usually occurs after birth, but sometimes it occurs in utero, and to such an extent that it seriously impedes parturition. It is, of course, identical in nature with that distension of the ventricles and thinning of the cortical substance to which we have had occasion to refer frequently in describing other cerebral and meningeal conditions, except so far as the ætiology is concerned.

(2) **Inflammation.**—When it is remembered that the phenomena of inflammation are intimately bound up with alterations of the blood-vessels and their contents, it is evident that in the case of the brain we shall have certain difficulties in approaching the subject. For the brain, so far as the true nervous substance is concerned, apart from the meninges, is practically avascular. So much is this the case, that it has been denied by some authors that true inflammation ever occurs. By others it is, however, held that, though rare, there is such a morbid condition as cerebritis or encephalitis. As a matter of fact, these authors include under the name conditions that are in many respects dissimilar to those constituting inflammation in other parts, so that it is safer, and probably more accurate, to hold that inflammation, in the common acceptation of the term, does not occur in the case of purely nervous matter. This statement is equally true in the case of the white and grey matters of the spinal cord, although we shall have to refer to one condition, at least, which has definitely close relationships to inflammation.

(*a*) **Cerebral abscess.**—Under certain conditions, of which the most important are disease of the middle ear and the bony parts of the nose, there occurs a collection of pus within the very substance of the brain itself. In the case of disease of the nose the abscess is generally found in the frontal region, but even then the formation of an abscess is rarer than the occurrence of a general suppurative meningitis when the intracranial tissues are affected. When the middle ear is the seat of disease the commonest situation for an abscess to be formed is the temporo-sphenoidal lobe, but we may also meet with an abscess in the cerebellum or in the parietal lobe. The size of the abscess varies considerably. In some cases it is not larger than a hazel-nut, but in others it may be as large as a Tangerine orange. It is usually situated at a minute distance from the surface of the brain, with the result that it may be broken into when removing the organ, or may be removed intact. It may be adherent to the petrous portion of the temporal bone owing to the existence of an adhesive meningitis, or it may lie perfectly separated, so far as macroscopic examination can determine, from the tissue to the disease of which it owes its very existence. Frequently the pus is contained by a very definite capsule, but sometimes the wall of the abscess is little more coherent than the softened pus in the centre.

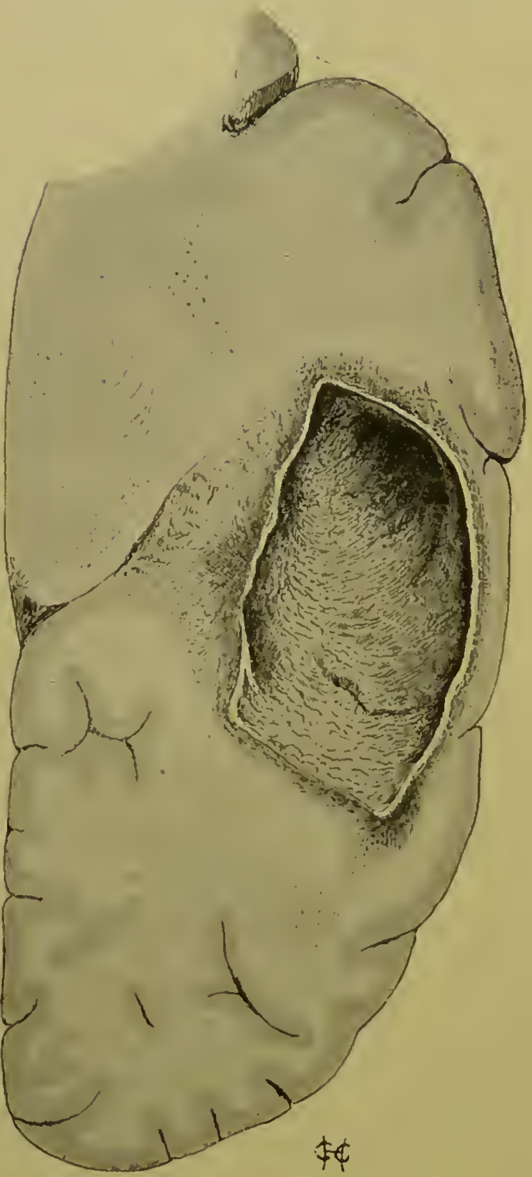

Fig. 159.—Cerebral Abscess (Temporo-Sphenoidal Lobe). × $\frac{3}{4}$.

The abscess cavity is smooth and has a well-defined wall. A narrow zone of brain substance lies between it and the meninges. Immediately around the abscess the cerebral substance is dark from the presence of disintegrated blood and other inflammatory materials. From a specimen in the St. George's Hospital Museum.

The pus of a cerebral abscess is generally characterised by an intense fœtor, and is usually greenish in colour. In the pus pneumococci have been found, and this fact is well in accordance with the fact that numbers of cases of otitis media also depend upon pneumococcal infection. The fœtor and the colour of the pus, however, probably depend chiefly, if not entirely, upon the presence of adventitious micro-organisms. Microscopically the pus almost always shows the presence of considerable numbers of characteristic 'pus cells,' and sometimes the pus is altogether of this—the acute—variety. But in the majority of cases, although a certain number of cells are present, the bulk of the pus consists of a granular *débris* and is of the chronic type.

The subsequent history of a cerebral abscess differs in different cases. In one it leads to death immediately from the pressure which it exerts upon vital parts of the brain, in another it induces a general suppurative meningitis, while in a third it may rupture into the lateral ventricle and cause a rapid death. One of the most important and interesting points about cerebral abscess is that it is practically certain that an abscess has often been in existence for a long time before it gives rise to clinical symptoms. That this is so we are, in many cases, certain from the characters of the pus contained in the abscess, but as to the length of time that it has been in the process of formation we are generally quite ignorant. Further, we are practically certain that sometimes the abscess has not increased in size for a considerable length of time before death. This is proved by the density of the capsule within which the pus is contained. It is not easy to understand how an abscess can have reached to the size of a Tangerine orange, for example, without giving rise to the slightest symptom, and it is equally inexplicable why an abscess which must have been present for months, to say the least, and is of considerable size, should suddenly light up and lead to profound symptoms which, if unrelieved, lead to death in a few days.

Although we sometimes meet with cases of suppurative meningitis which can be explained upon no other supposition than that they are the results of a pneumococcic infection, this is never the case with a definite cerebral abscess. In the case of this pathological condition we can always find a certain amount of disease either of the ear or nose, or occasionally of some other part intimately connected with the encephalon, and we can usually find some distinct evidence of disease of bone.

(β) **Tuberculosis.**—The principal form in which tuberculosis affects the brain is by way of tuberculous meningitis. But in addition to this condition, in which the tubercles are miliary, we sometimes meet with definite caseous masses in the substance of the brain which are the results of tuberculous infection. These masses are similar and analogous to the caseous masses which occur within the spleen and other organs. They may be present in any part of the brain, but are commoner in the cerebellum than elsewhere. They vary in size, but are usually about the size of a hazel-nut. They form definite tumours, and indeed constitute the commonest variety of 'cerebral tumour' in children. They are more frequently met with in children than in adults, and are decidedly rare in persons above the age of twenty.

Macroscopically, tuberculous masses present the ordinary appearances of a caseous mass. They are frequently surrounded by a denser part which approximates towards a capsule, but in reality no definite capsule is formed, the denser portion consisting, in the majority of cases, of nothing more than a tuberculous granulation tissue which is on the point of becoming caseous. It is not common for the surrounding portions of a caseous mass to present, histologically, the appearances of tuberculosis, although this may be the case. More generally we find only a collection of small round cells, with a few elongated cells, giant cells being completely absent, or found only after a prolonged search. Macroscopically, this outer zone of the caseous mass often has a semi-translucent appearance, similar to that surrounding a mass of tubercles in the lung or other part. In a good many cases the caseous masses lie so close to the surface of the brain that it is probable that they have originated in connection with the membranes, and have pushed aside the cortical substance of the brain rather than have originated in it. In spite of this fact, however, it is probable that in a certain number of cases the formation of the tuberculous focus is truly cerebral and not meningeal.

As a rule, a tuberculous mass gives rise to symptoms only by reason of the pressure which it exerts upon neighbouring structures. This is, however, almost always sufficient to lead to the death of the patient. Whether as the result of alterations induced in the optic disc or as the result of interference with the visual apparatus at the corpora quadrigemina, tuberculous masses, like other solid tumours of the brain, are liable to lead to blindness.

(γ) **Syphilis.**—Syphilitic disease of the brain shows itself under two forms. Either it is present as an endarteritis, and this is the commoner, or definite gummata are present. In either case it may be said that the meninges rather than the actual brain substance is the part primarily affected. Indeed, it is doubtful whether syphilis ever affects the brain substance without origination in the meninges. So far as the affections of the blood-vessels by syphilis are concerned, we shall consider them in connection with other alterations of the cerebral vessels; and as far as gummata are concerned, all that has been said with regard to the caseous masses of tuberculosis is equally applicable to the caseous masses of syphilis, so far as the macroscopic and microscopic appearances are in question. It must be said, however, that the parts of the brain which are liable to be the seat of gummata are not those which are liable to be the seat of tubercle. Neither is the age of the patients affected the same. For whereas the cerebellum is frequently the seat of a tuberculous caseous mass, it is very rarely the seat of a gumma, the commonest situation of which is the base of the brain, especially about the crura. As a result, various ocular paralyses are common in cerebral disease of syphilitic origin which are not common, or not equally common, in tuberculosis. With regard to the age question, it is clear that the patients who are the subjects of gumma are likely to be about twenty years older than those affected by tubercle, from thirty to forty years of age being the commonest age for the occurrence of gummata.

(3) **New-growths.**—While we are dealing with the solid formations within the brain it will be convenient to mention the true tumours which are found. Of these the endothelioma and the glioma are the most common. The **endothelioma,** as will be readily understood, generally arises in connection with the meninges. It may, however, arise in connection with the ependyma of the ventricles, or the entire pineal body may be replaced by an endothelial growth. The tumours may be as large as a Tangerine orange.

The effects of the endotheliomata are principally those of pressure, and therefore we find that the cortex is depressed and displaced, and not infrequently has undergone a considerable amount of pressure atrophy. The displacement is often clearly shown by the deviation of the longitudinal fissure from the middle line, while the corpus callosum is equally depressed upon the side of the tumour. It is generally easy to draw a macroscopic line between the tumour itself and the underlying brain substance, but this distinction cannot always be made with similar ease under the microscope.

In the case of the **glioma** we have a tumour which almost always lies in the very substance of the brain itself, and, indeed, arises in connection with the neuroglia. It is therefore much more difficult to distinguish, both macroscopically and microscopically, the actual limits of the tumour. Sometimes the tumour is rather to be recognised by the difference in consistency than by the presence of a definite swelling, though the microscope quickly reveals the actual nature of the altered part.

True gliomata are of rather rare occurrence. Far more common, though still less common than endotheliomata, are glio-sarcomata. In these growths there is a resemblance to both types of tumour, but, as a rule, the tumour verges rather towards the sarcomatous type than to the gliomatous. Indeed, in a large number of cases the amount of sarcomatous tissue is so considerable that it is only after a prolonged search that a small portion of glioma is found. The cells of a glio-sarcoma are usually of the small round variety.

True sarcomata of the brain are rare, and are almost always secondary. They may be found in any part of the brain. When primary, sarcomata arise generally in connection with the meninges, and only affect the brain itself secondarily, whether by direct extension or by the formation of metastatic deposits. Whether primary or secondary, the growths have the ordinary characters, both histological and clinical, of the sarcomata generally. It has already been noted that, in the case of the pineal body, we may meet with sarcomata of the melanotic variety. These may be more or less localised, or they may be diffused throughout the meninges as a general blackish thickening.

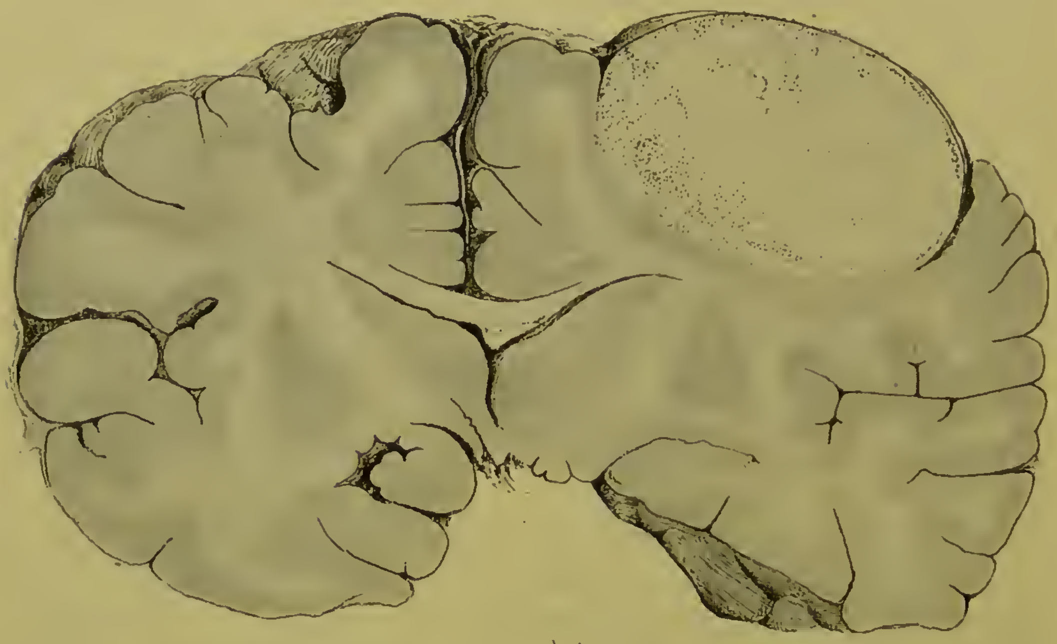

Fig. 160.—Cerebral Tumour. × $\frac{2}{3}$.

An ovoid mass which has originated in the membranes is situated in the arm area. Inferiorly it is fairly distinct from the brain substance, and a thin layer of grey matter is seen beneath it. It is covered by the pia mater. The compression of the brain on the side of the tumour is well seen by the flattened convolutions and the narrow sulci between them. The corpus callosum is distorted. The growth was an endothelioma.

Carcinoma is said to occur in the brain only as a secondary deposit; and although this statement is certainly very nearly true, it must, perhaps, not be taken as absolute. At any rate, in one case seen by the author the histological characters of the wall of a cyst of the cerebellum which caused the death of the patient were those of a typical columnar-cell carcinoma of the villous type. When the carcinomatous nodule is secondary it may be of any of the ordinary types.

Results that are clinically indistinguishable from those produced by solid tumours of the brain are also produced by the hydatid forms of various parasites, of which the Cysticercus cellulosæ is the commonest. Ordinary hydatids of the brain are very rare.

(4) **Affections of the cerebral arteries and their branches.**—We have already referred to the morbid conditions affecting the meningeal veins and the venous sinuses, but it is somewhat more convenient to consider the affections of the arteries in connection with the brain substance itself than in connection with the meninges.

The three most important affections of the cerebral arteries are embolism, thrombosis, and rupture. The morbid conditions underlying these are different. For in embolism the vessels of the brain itself may be perfectly healthy, whereas in cases of rupture and thrombosis the vessel walls are invariably more or less diseased.

The subject of **embolism** may be dismissed with a very few words in a work on pathology, although in works upon clinical medicine it is a subject of the greatest importance. It generally results from the detachment of a particle of fibrin from a vegetation upon a cardiac valve, that is the seat of organic disease. As might be inferred, the valve affected must be either the aortic, which is most commonly the case, or the mitral. Owing, in part, to the anatomical arrangement, the clot is generally carried into the middle cerebral artery on the right side. As this vessel is of the terminal variety and supplies the central parts of the brain, the result of the lodgment of an embolism is always the production of a certain amount of softening (unless the shock is so profound that death occurs very rapidly after the accident), and sometimes the softening concerns almost the entire mass of the basal ganglia on the affected side. Where the clot is very large the result of the embolism may be somewhat unexpected. For the interference with the circulation may be so severe that there occurs secondarily an enormous congestion in the veins that normally return the blood from the area supplied by the obstructed artery. The pressure within these veins may be sufficiently great to rupture one or more of them and lead to an extensive extravasation of blood beneath the pia mater. This extravasation may extend over the entire base of the brain, and may even encroach for a considerable extent over the sides and vertex.

When the obstructed artery is small, the softening that results is of the white variety; but when the embolus becomes lodged in the main artery, such softening as occurs, besides being very extensive superficially as well as deeply, is almost always of the red variety.

The result of the embolism naturally differs if it has originated in connection with the ulcerative form of endocarditis. It may then lead to the formation of a definite abscess of the brain, which is as distinctly pyæmic in its character as the abscesses formed in other parts under similar conditions.

Thrombosis of the cerebral arteries occurs under the same conditions as lead to thrombosis of arteries elsewhere. That is to say, the chief factors in causing it are feebleness of cardiac action and alteration of the vessel wall. Either of these conditions may operate independently of the other, but it is far the commonest for alteration of the arterial wall to be present, and in a certain class of case it is the sole effective agent.

Thrombosis of the cerebral arteries may result from either atheroma or syphilitic endarteritis, and, as might be supposed, the patients who suffer from the condition are to be divided, so far as age is concerned, into two classes. Those patients who are affected with thrombosis as the result of a syphilitic endarteritis are usually men in the prime of life, while those in which the primary arterial affection is atheroma are old.

Syphilitic endarteritis shows itself in the characteristic way when it affects the cerebral arterioles. It leads, therefore, to the formation of a low form of granulation tissue which shows a great tendency to undergo central caseation, and which is present locally at some point in the vessel wall. The inflammatory material, which is in reality nothing more than an early gumma, does not surround the entire wall of the vessel at the point at which it is present, but it leads to a projection of the wall at that point into the lumen of the vessel. At first covered by the vascular endothelium, it soon loses this coat, and the narrowing of the lumen, combined with the slackening of the blood stream at the point of stenosis, is ultimately sufficient to lead to a sudden and complete thrombosis of the artery as far as the branch above the stenosis and for a variable extent below. Any of the arteries of the brain may become the seat of syphilitic endarteritis, but it is commonest to find it affecting either the middle cerebral artery or the arteries entering into the formation of the circle of Willis, or the basilar artery. In the latter position the change is of fairly common occurrence, and is of especial importance by reason of the intensely important parts with which the basilar artery lies in immediate relation, and which draw their nourishment from it. Cases of thrombosis of the basilar artery probably always show a sudden onset, and it is very doubtful whether recovery ever takes place. As a rule, the patient dies within a few hours. The complete absence of noticeable lesion, except the fatal one, is often a most characteristic feature of the case, and even then the area of thrombosis may not be larger than the head of a fair-sized pin.

Atheroma of the cerebral arteries does not always lead to thrombosis—and fortunately so, for it is of very common occurrence, particularly in persons who are the subjects of granular kidney. It shows itself in its earlier stages by a distinct increase in the rigidity of the vessels. This is very noticeable in the case of the internal carotids. In the normal brain with normal vessels these arteries collapse when they are cut through in order to remove the brain; but when they are the seat of atheroma, quite apart from any other macroscopic change, they are found to stand up rigidly open. As a rule, too, their walls are thickened, and this is in agreement with the fact that chronic fibrosis of the kidney is liable to be accompanied by arterio-sclerosis, a frequent forerunner of atheroma. When the atheroma is distinctly recognisable, it generally shows itself by the presence of irregular opaque white patches in the wall. At an early stage these patches consist of intimal cells which have undergone fatty degeneration, but later they become rigid owing to the deposition of calcareous salts. In a severe case we may find both middle cerebral arteries and a large number of their branches as completely calcareous as are the vessels in a limb which has undergone senile gangrene. In such a case we are certain to find that the lumina of the vessels are filled with thrombus; and although the question is sometimes not fully beyond doubt, it is often certain that the thrombosis was of ante-mortem occurrence and played a considerable part in occasioning the death of the patient.

Rupture of the cerebral arteries may, of course, be of traumatic origin or spontaneous; it is of the latter alone that we shall speak here.

When a cerebral artery ruptures it is generally, but not invariably, the seat of disease. It is clear that rupture may be brought about either by the action of a fairly normal arterial pressure upon a diseased vessel wall, or by the action of an enormously increased arterial pressure upon a normal vessel wall. Examples of the latter condition are of very rare occurrence, but they may be seen in cases of chorea and other convulsive diseases and conditions. The hæmorrhages are then likely to be small, and may be met with in any part of the brain, but especially in the white matter.

So far as ordinary cases of cerebral hæmorrhage (apoplexy) are concerned, the commonest alteration of the vessel antecedent to rupture is the formation of a minute **aneurysm**. This is the result of atheroma, the aneurysm forming on the cerebral artery in exactly the same way as it forms on the aorta under similar conditions. As a rule, more than one aneurysm is found when they are present at all, but when rupture has taken place it is generally difficult, and often impossible, to find the actual aneurysm which has given exit to the blood.

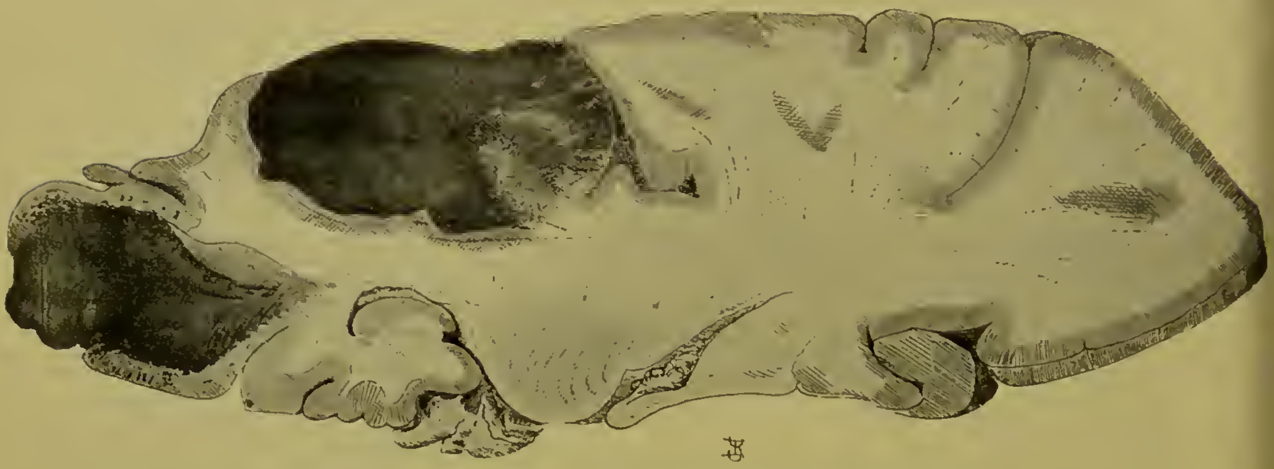

Fig. 161.—Laceration of Brain (Traumatic). × $\frac{2}{3}$.

A slice of brain from front to back showing two large lacerations into which hæmorrhage has taken place. The lacerated vessels have been meningeal. The narrow grey zones beneath and around the clots are not grey cerebral substance, but white matter which has been infiltrated and discoloured by blood and blood pigment.

The vessels which are particularly liable to give way and occasion a cerebral hæmorrhage are the lenticulo-striate branches of the middle cerebral artery. These vessels are for a considerable part of their course relatively unsupported by the tissues in which they lie, and therefore rupture more readily whenever the pressure within them is suddenly raised. That the actual rupture is often due to the sudden increase of pressure is shown by the fact that a cerebral hæmorrhage is often induced by the straining of defæcation, or on attempting to rise from the bed in the morning.

The size of hæmorrhages varies enormously. In some cases

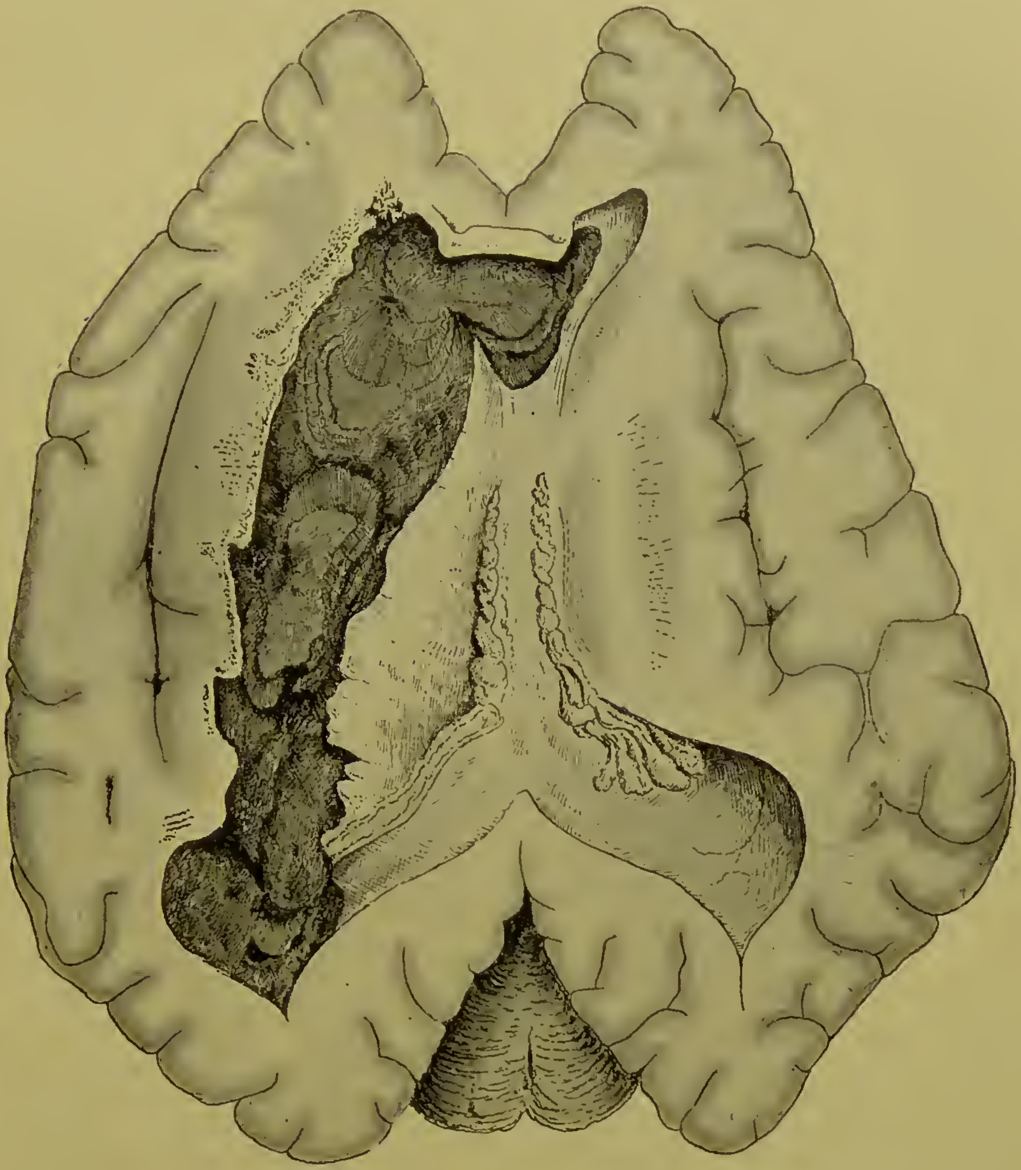

Fig. 162.—Cerebral Hæmorrhage. × $\frac{2}{3}$.

A hæmorrhage has taken place which has torn up the corpus striatum and has ruptured into the lateral ventricle. The entire left lateral ventricle is distended and filled with clot, and a certain amount of clot is seen in the anterior cornu of the right lateral ventricle. The posterior cornu of the right lateral ventricle is distended, and was filled with bloody cerebro-spinal fluid and serum. The bulging of the surface of the left hemisphere caused by the clot is well seen.

they are so small that they lead to no symptoms, and are discovered only at the autopsy. This is, of course, particularly the case when they have taken place into a part of the brain which is not primarily concerned with the maintenance of life. On the other hand, they may entirely plough up the greater part of one hemisphere, and, rupturing into the lateral ventricle, may fill this and the ventricle on the other side. As a rule, the part which is principally affected is the anterior part of the basal ganglia on one side. The internal capsule therefore becomes completely disorganised, and hemiplegia results.

Hæmorrhages also take place with considerable frequency into the pons, and are then, as a rule, accompanied by special symptoms, of which the occurrence of pinhole pupils and a rapid rise of bodily temperature are the most common and significant. It is rare for a pontine hæmorrhage to be confined to the substance of the pons. Far more generally it ruptures through the cortical portion at some point. Pontine hæmorrhages, too, may be associated with hæmorrhage into the basal ganglia.

When a hæmorrhage has taken place, the subsequent history of the effused blood largely depends upon the quantity which has been poured out. Unless death is immediate, coagulation takes place, and even then by the time we have opened the head there is found a clot at the seat of hæmorrhage. The clot is sometimes very firm, but there are always looser parts which fall away when the brain is opened. In the case of a large hæmorrhage, the side upon which the extravasation has taken place is always discernible by the bulging of the cortex and the flattening of the convolutions. When the blood has escaped into the lateral ventricles there is always present a certain amount of blood-stained fluid at the base of the brain.

In cases such as the above it can hardly be said that the effused blood undergoes any other change than coagulation, but when the hæmorrhage is of small size and does not lead to death it may be found subsequently in the form of a cyst with a certain amount of blood-staining of the walls. The presence of crystals of hæmatoidin in the surrounding brain substance indicates the nature of these cysts, but in some cases we find cysts which have clear colourless contents, and concerning the origin of these, although we believe that they are frequently the remnants of old hæmorrhages, we are in some doubt.

The effects of a hæmorrhage may be far greater than those which have been described above. For the immediate result of the hæmorrhage is to sever the connection of certain medullated fibres from the nerve cells with which they are normally united. Hence there may occur a certain amount of sclerosis after the earlier degenerative changes of the fibres have taken place.

Into these changes we shall not enter here, as they become chiefly significant in connection with morbid conditions of the spinal cord.

III. THE SPINAL CORD

Degenerative changes of the cord, in the sense in which the term ‘degeneration’ has been used previously, are of infrequent occurrence. It is true that the pigmentary change in the large ganglion cells to which attention has already been several times directed, is found to the most marked extent in the cells of the ventral horns. It is also true that the cord is one of the regions in which the degenerative change of sclerosis is met with. But of fatty degeneration, lardaceous degeneration, &c., we hardly ever meet with primary examples, and they may be dismissed without further remark.

Atrophy of the cord is almost always unilateral, and we are even more likely to find that the condition is confined to some particular tract of the cord. It is always associated with some other antecedent change, of which a disappearance of the cells of the ventral horn is the most important and common. To the conditions under which this morbid state occurs we shall have to refer more in detail later. Atrophy also occurs over a localised area or tract when some part has been removed. Thus, after an amputation of the lower or upper limb we find that the corresponding part of the cord has undergone shrinkage. This is nothing else than a disuse-atrophy.

Myelitis.—Although it is as doubtful in the case of the spinal cord as in the case of the brain substance proper whether a true inflammation occurs, there is no doubt that a condition exists which is associated with marked changes in the meninges of the cord, and in the actual nervous substance itself, which is in part inflammatory, and therefore is fairly termed myelitis.

This condition consists principally in a softening of the cord over some part, principally a portion in the dorsal or the lumbar region. So far as the cord itself is concerned, the change consists merely in a softening of the white variety, and all differentiation into the tracts, or even into grey and white matter, is quickly lost. It is not possible to recognise the change easily with the eye, but an attempt to divide the cord in the ordinary fashion quickly shows that it has entirely lost its normal consistency and has become converted into a substance resembling cream in its appearance and density. Such an area of softening extends for a greater or shorter distance along the cord, and almost always affects it throughout its entire sectional area, so that the term 'transverse myelitis' is generally applied to it. At the point of greatest change this alteration is very marked, but at a little distance the cord generally has a more or less normal appearance to the naked eye. The meninges are frequently reddened in the immediate neighbourhood of the focus of softening, and there is little doubt that they are the seat from which the morbid process primarily extends in the majority of cases. Whether the softening commences sometimes in the substance of the cord it is difficult to say, but on the analogy of the cerebrum there is no reason why it should not do so.

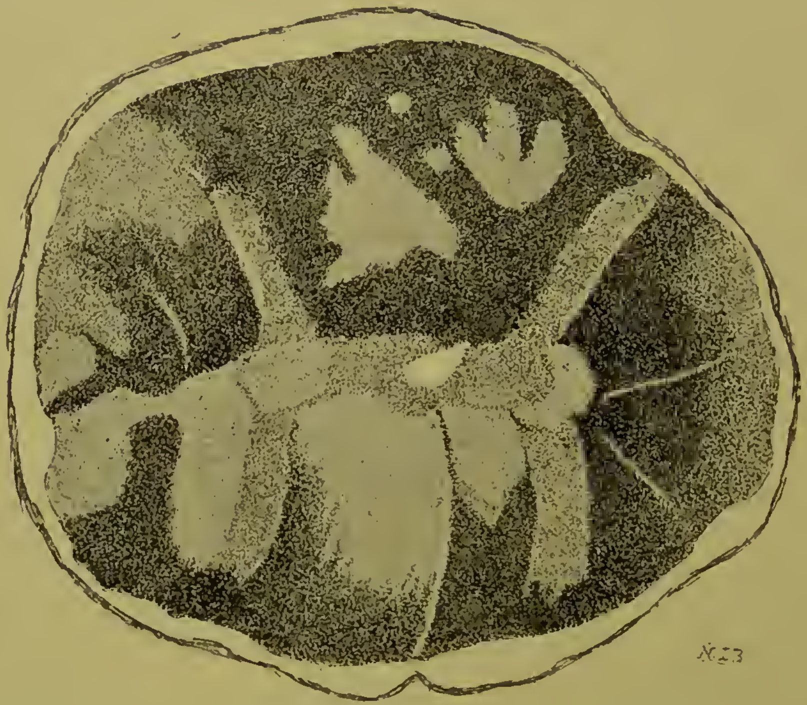

FIG. 163.—SECTION OF CORD IN A CASE OF TRANSVERSE MYELITIS. × 6.
The section is taken from the dorsal region of the cord, the lesion itself having been in the lumbar region. Irregular patches of degenerated (unstained) fibres are seen in all parts of the cord, while degenerative changes have taken place in the grey matter also. The section would also serve to show the irregular degeneration that occurs in disseminated sclerosis. Stained by Pal's modification of Weigert's method.

Myelitis has important effects upon parts of the cord both higher up and lower down. However much the cord may seem to be unaltered at a little distance, to the naked eye, it is always possible to determine, on staining by appropriate methods, that there is a more or less extensive degeneration upwards and downwards. This degeneration shows itself not only by changes in definite tracts, but even more commonly by a more or less irregular degeneration which does not seem to be confined to definite tracts. In addition to this, there will always be present a considerable number of degenerated fibres in the midst of white matter that is otherwise but little altered. The degeneration diminishes in extent as we pass upwards in the afferent tracts of the cord, but the motor tracts, which pass downwards, are degenerated in their entirety.

It is principally by Marchi's method that we find evidences of the degeneration. It shows itself by the presence of broken-down medullated substance which stains black by the osmic acid in the reagent. This change is visible when, as is usually the case, the patient lives for only a few weeks after the onset of symptoms. In the rare cases in which the patient lives longer, Marchi's method is less valuable, and staining by Weigert's method or any of its modifications affords better evidence of the changes which have taken place. By this time the changes are chiefly or entirely sclerotic. *Above* the lesion the chief changes are, of course, found in the posterior columns and in the direct cerebellar tract; *below* the lesion, it is the anterior and lateral tracts which suffer most.

At the site of the lesion itself, the microscopic changes are profound. The greater part of the section consists of granular *débris*, and perhaps the only information as to the nature of the tissue from which the section was taken is obtained from the fact that a very few, greatly disorganised, remnants of anterior cornual cells are present. Moreover, these are recognised rather from the facts of their position and their intense staining with methylene blue than from any other property. Beyond these cells, the only other formed elements will probably be a certain number of leucocytes, perhaps a few 'Gluge's corpuscles,' and a small quantity of extravasated blood or isolated red blood corpuscles.

Spinal meningitis.—With the exception of that meningitis which is induced by accident or other traumatic cause, the chief variety of spinal meningitis is that which coexists along with an inflammation of the cerebral meninges, and which we have already described under the name of cerebro-spinal meningitis. To this no further reference will be made.

The other important varieties of spinal meningitis are those which occur as the result of tuberculosis or syphilis. They are mentioned in connection with myelitis because it is evidently impossible that any but the most minute inflammation of the meninges can exist apart from the presence of changes of the spinal cord.

Of the two varieties of meningitis which have just been mentioned, that occurring as a result of **tuberculosis** is the commonest and most important. The tuberculosis generally originates in connection with one of the vertebræ, and the degenerated products press on the exterior of the spinal meninges and subsequently affect them and the enclosed cord as well. The change in the cord consists in a myelitis which differs little in its macroscopic and microscopic appearances from the acute variety which has been described. There is, however, a tendency for the cord to be more considerably flattened in some one direction owing to the greater length of time which has been occupied in the process of inflammation. The accumulated material between the bone and the meninges, and the meninges and the cord, is that caseous material which is always found in connection with tuberculosis. At a little distance from the focus of accumulation definite microscopic evidences of tubercle may be found. From its association with spinal caries the condition is principally met with in the dorsal or the lumbar regions of the cord. In the cervical region, although the condition occasionally is found, it is much rarer, partly by reason of the greater rarity with which the

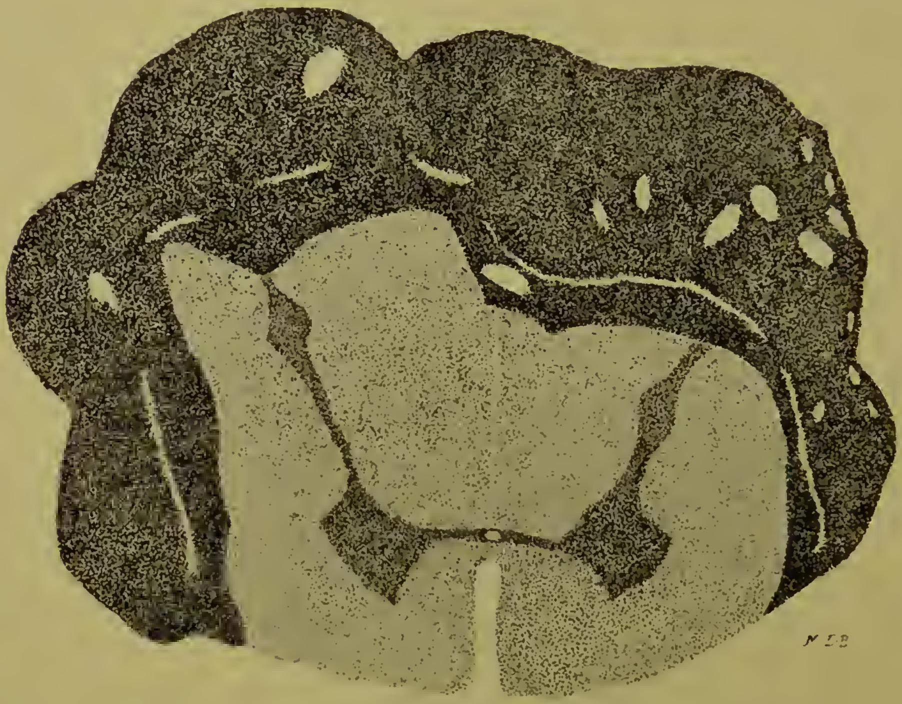

Fig. 164.—Section of Spinal Cord being invaded by Sarcoma of Spinal Meninges. × 6.

The section is from the cervical region. The dark mass consists of sarcoma cells which have in places undergone degeneration and formed small cysts. The growth is invading the cord posteriorly. Stained with alum-carmine.

cervical vertebræ are affected with tuberculosis, and partly because the spaces between individual vertebræ are larger in this part of the column.

Cases of **gumma** of the cord generally originate in the spinal meninges. The characters of the gumma itself offer no peculiarities, and the principal effect of the accumulation of degenerated material lies in the pressure which it exerts upon the cord. Although gumma is occasionally met with, it is far commoner for syphilis to affect the cord in other ways. Of these the majority are chronic, but if the syphilitic disease of the cord is acute, it generally shows itself in the form of a transverse myelitis of the kind which has already been described.

In this connection we may mention the **solid tumours** of the cord, for the changes to which they give rise are practically identical with those produced by gummatous and tuberculous deposits. In the vast majority of cases they are secondary, and sarcomatous. In a few cases, however, they are primary, and then they most commonly originate in connection with the spinal meninges, and are either sarcomatous or endotheliomatous. Conditions which commence in the bones of the vertebral column or in parts adjacent thereto may, of course, involve the cord by direct extension, but these we need not discuss. Primary tumours of the cord itself are extremely rare, and are almost always of a gliomatous nature.

Under almost the same heading comes hydatid disease of the cord, so far as the changes are concerned which it produces. The condition is peculiarly interesting in that the hydatids are loose and are dispersed irregularly throughout the entire length of the cord, though not in its substance. There is therefore no trace of a mother cyst, but all the brood capsules are quite free.

In the case of the morbid conditions which have just been described there is a general uniformity in the pathological changes which are produced in the cord itself. The first and most characteristic change consists in a flattening. This flattening may not be accompanied by any other change in the cord itself, if it is not very severe. But when it is severe, it is always associated with a greater or smaller amount of degeneration. And as the degenerative changes are the cause of other changes (e.g. of the kidneys) which rapidly lead to death, in most cases, the cords of those who have died as the result of a tumour of the cord, or a tumour of the meninges which presses upon the cord, show large tracts of early degeneration when stained by Marchi's method. The more chronic and later change of sclerosis is much less commonly seen. At the seat of principal compression the cord is often flattened so much that it is ribbon-like, and offers no trace of resemblance, either macroscopically or microscopically, to the normal. In a considerable number of cases the cord, when examined after death, shows a much greater degree of alteration than would have been expected from a consideration of the clinical symptoms.

The white matter. The scleroses.—It will be remembered that we have on several occasions referred to the change which constitutes sclerosis of the spinal cord, and have said that it consists in the replacement of certain of the nervous elements by a dense tissue which is apparently derived from the neuroglia and closely resembles ordinary fibrous tissue in many of its characters. This sclerotic tissue is found in a variety of situations in the cord, but it is almost exclusively confined to the white matter, and in this part it follows certain definite tracts. Thus we have a sclerosis which is almost entirely confined to the postero-median and the postero-external columns; another which is found in the anterior column of one side and an associated tract in the lateral column of the other side. These constitute the two best recognised varieties of sclerosis. In another variety there is a sclerosis bilaterally placed in the lateral columns; this is a well-

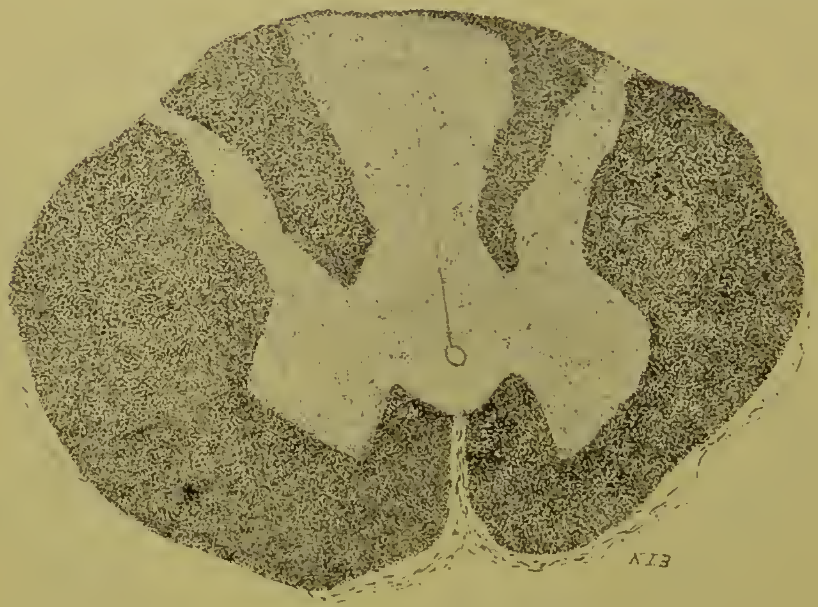

FIG. 165.—SECTION OF SPINAL CORD SHOWING SCLEROSIS OF POSTERO-MEDIAN COLUMNS. × 8.

From a case of tabes dorsalis. The postero-median columns in this, the dorsal region, are completely sclerosed. Other parts of the cord seem to be normal. Stained by Pal's modification of Weigert's method.

recognised variety, but is less commonly met with than either of the two which have been previously mentioned. In addition we meet with localised patches of sclerosis, each of which is associated with a secondary localised tract-sclerosis which proceeds upwards or downwards for a longer or shorter distance in the cord. Then again we meet with scleroses which are the result of disuse, as for example those which occur when a limb has been amputated for disease.

In each of the conditions that have been mentioned above it is clear that a more or less definite collection of symptoms will be produced. These constitute distinct diseases. Thus it is in the disease known as **tabes dorsalis** or **locomotor ataxy** that we meet with a sclerosis of the postero-median columns; and although this change is not absolutely confined to that disease, but naturally occurs whenever the afferent mechanisms are greatly interfered with, yet in conjunction with certain other nervous changes in the cord, and in the nerves themselves, it becomes quite characteristic. So, too, sclerosis of the anterior and crossed pyramidal tracts results from a lesion in the brain itself, and is frequently the late result of a cerebral hæmorrhage which has not led to death. For this reason scleroses in these regions are generally associated with sclerosis of the crusta of one crus. If the primary disease has been in the motor centres on the cortex, it may be possible to distinguish tracts of sclerosis which pass through the corona radiata, the internal capsule, and the crus, track through the pons, and divide at the decussation into the anterior and crossed lateral pyramidal tracts. These tracts of sclerosis pass for a varying distance down the cord, and become smaller and smaller as one passes downwards. In the upper dorsal region the anterior pyramidal tract has disappeared entirely. In the condition in which the lateral tract on each side is affected with sclerosis we have the collection of symptoms which constitutes the disease known as **lateral sclerosis**. It is quite distinct from other forms of nervous disease, and is clinically easily recognised. In those cases, too, in which numerous foci of degeneration are present in the cord with the tracts of sclerosis which emanate from each, we have a distinct disease which is known as **disseminated** or **insular** or **multiple sclerosis.**

In the varieties of sclerosis which we have just mentioned it is impossible to point to any stage as being early in the condition, for the sclerotic tissue is always fully formed. The only differences that we can see lie in the different degrees to which the tracts of the cord have been involved. It is, however, certain that when a degeneration of the medullated fibres of the cord takes place, if the patient survives for a sufficient length of time, the place of the degenerated fibres is taken by a sclerotic material different in no respect from that which is present in the primary scleroses.

The grey matter.—Affections of the grey matter of the cord almost entirely resolve themselves into changes which concern the large multipolar cells of the ventral horns. Here the change is of one kind only, so far as is at present known, although it may be either acute or chronic. In the former case we have produced the disease known as **acute anterior poliomyelitis** or **infantile paralysis**; in the later we have **chronic anterior poliomyelitis** or **progressive muscular atrophy**. In both cases, therefore, the clinical character of the disease which results is an atrophy, combined with a paralysis of muscles supplied by the motor nerves which originate in the affected cornual cells.

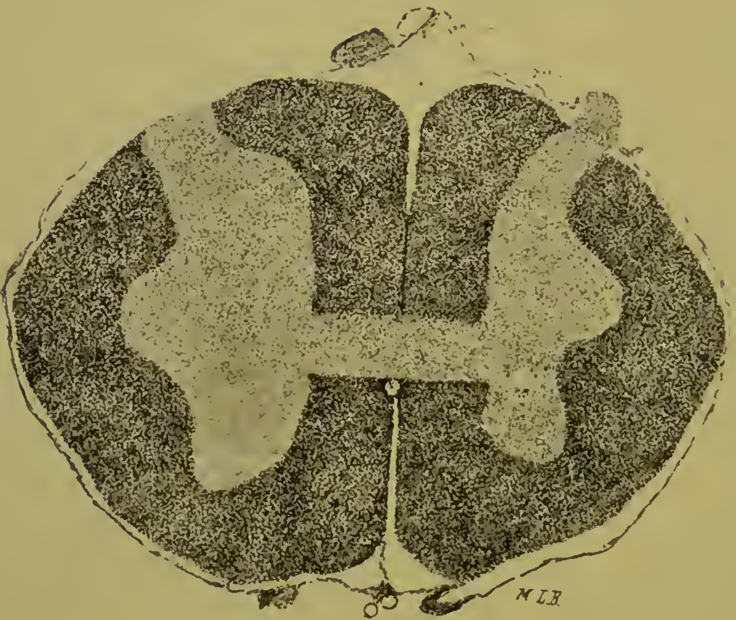

Fig. 166. Section of Spinal Cord in Infantile Paralysis. × 8.

The ventral or anterior cornu on the right side of the figure is greatly diminished in size, and a clear space is seen in it where complete degeneration has taken place. The white matter of the cord immediately beneath the affected horn is flattened owing to the relative absence in it of the anterior roots. The commissure and central canal have accidentally been mis-drawn. Stained by Pal's modification of Weigert's method.

The changes that occur in these forms of disease are chiefly to be recognised by their late results. At an early stage it is doubtful as to the actual alterations which take place, for the diseases in question do not tend to destroy life. But after the process has been in play, and the condition has proceeded to a quiescent state, it is found, on the occurrence of death from some other cause, that the entire ventral horn corresponding to the affected part has undergone shrinkage, so that it is definitely smaller than its fellow. Even with a low power of the microscope, or with the naked eye, it is possible to see that the large multipolar cells have undergone a diminution in number, while such as are present are smaller than normal and generally stain more deeply. A somewhat higher power of the microscope shows that many of the cells are shrunken and lie in larger perineuronal spaces than normal, while they are supplied with a smaller number of terminal arborisations than normal, or are completely devoid of them, and also show a distinctly pathological axon. Further, the cell has lost almost entirely, or entirely, the 'Nissl bodies,' which are normally present in large numbers in these cells. At an earlier stage of the disease it may be found that there are definite hæmorrhages into the substance of the anterior horn, while blood corpuscles may very possibly be found in the perineuronal spaces themselves. At the same time, the neighbourhood of the altered cells is invaded by a considerable number of leucocytes. The white matter of the cord does not generally show any pathological change, but the capillaries may be fuller of blood than normal, and there may be a few small extravasations. Naturally, if the process has been very extensive, and has therefore involved a considerable number of the ganglion cells over a large tract of the cord, a corresponding diminution in the size of the white columns at the points at which the axons normally pass out is observed, as is also a diminution in the size of the anterior nerve-roots themselves.

While we are dealing with the changes in the large ganglion cells, mention may be made of the most characteristic acute change which is known to affect them. It concerns the distribution of the chromatophilic substance which is normally collected into the masses known as 'Nissl bodies.' Under certain conditions the cells, when stained by Nissl's method, fail to show the presence of the bodies, but, on the contrary, are stained diffusely throughout. The best example of a condition in which the change occurs is hyperpyrexia, and it appears fairly certain that this point constitutes a difference between hyperpyrexia—a febrile state—from hyperthermia—a condition in which, although the bodily temperature is raised, it cannot be said that 'fever' is present. In typhoid fever also the change has been noted; but although experiments have been made with reference to the subject, it has been found that in such diseases as tetanus and diphtheria, which have especial tendencies to affect the nervous system, no alteration of the cells in this respect takes place. The subject is one upon which a great deal more information is needed.

In addition to the changes which have been mentioned above as affecting the white and grey matter of the cord, we often find in spinal cases which have died after a short illness a number of minute lesions which differ almost infinitely. These lesions consist for the most part in changes which we can best sum up as being included under the term ‘inflammation.’ At all events they are almost always vascular, and affect principally the capillaries and other small vessels that traverse both the white and the grey matter. The vessels may simply be fuller and more conspicuous than normal, or there may be definite hæmorrhages, or, again, there may be small local accumulations of leucocytes (usually lymphocytes), or the perineuronal spaces are abnormally large or are filled with red blood corpuscles or with leucocytes. These changes may be more or less confined to one region of the cord, but it is generally very difficult to correlate them with the symptoms which have been present in life.

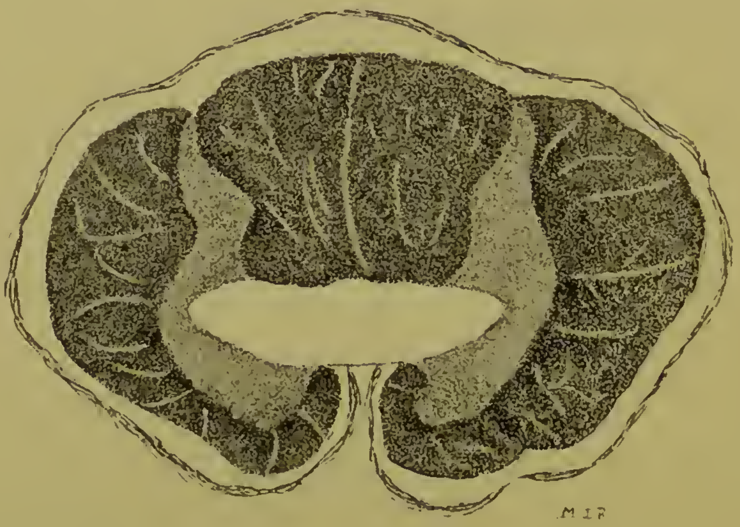

Fig. 167.—Section of Spinal Cord showing Hydromyelia. × 6.

Dorsal region. The central canal was widely dilated in fusiform fashion in the entire dorsal and in part of the lumbar region of the cord. There was no evidence of new-growth. The grey matter of the cord is distorted. The numerous clefts in the white matter are probably artificial. There is apparently no grey or white commissure.

The central canal.—Normally the central canal of the cord is of inconspicuous size even in the cervical portion of the cord, where it is largest. But under certain conditions it undergoes changes which cause it to become greatly enlarged.

The simplest of these changes is that in which the canal is much larger than normal throughout the length of the cord, but is otherwise normal in its constitution. This condition is known as **hydromyelia.** In it, the canal may occupy the entire commissure, or, indeed, the grey matter of the two sides of the cord may not appear to be in communication. Nevertheless, the microscope always shows that there is a certain, if small, amount of grey matter surrounding the dilated canal. The effect of the dilatation is shown in an alteration of the arrangement of the white and grey matters, and an alteration in the shape of the cord. In any case, however, the cord itself is symmetrical in shape. In the condition which is known as **syringomyelia**, the dilatation of the central canal is brought about by other means, for it results generally from the softening of a new-growth (probably a glioma) which has formed in the grey matter of the cord in close proximity to the central canal. Hence in syringomyelia there is not the same tendency for the central canal itself to be symmetrical, and for the same reason the transverse section of the entire cord is often irregular.

Both hydromyelia and syringomyelia usually affect the cord for a considerable portion of its length. The principal situations in which they are found are the dorsal and the lumbar regions, and the dilatation has generally a more or less fusiform shape, so that the dilated cavity tapers off above and below.

In **spina bifida** we have another morbid condition of the central canal with an origin different from that of the conditions which have been mentioned. For spina bifida is definitely due to maldevelopment, and depends upon a failure to unite of the transverse portions of certain of the vertebræ. The commonest situation in which the condition occurs is the sacral region, but it may occur practically anywhere, and in cases of extreme malformation we may meet with a failure to unite of the transverse arches throughout the entire length of the cord.

In a typical case of spina bifida the child has a sacral swelling, which fluctuates, and which is sometimes only covered by the skin, but is sometimes covered by a small amount of deeper tissue. At the bony attachment of the swelling it may be felt that there is an opening into the vertebral column. The swellings vary considerably in size. In one instance it may be as large as a chestnut, in another it may be as large as an orange. This variation naturally depends upon the number of vertebræ that are concerned in the malformation. The condition is always noted in infants, and in the cases of the larger swellings it generally terminates fatally within a very short time, owing to the extension of inflammation to the interior of the sac and its promulgation to the entire cerebro-spinal fluid. This result may depend upon surgical measures, but it will probably occur in their absence, at all events, in the case of a spina bifida of any dimensions, owing to the poor nutrition of the skin covering the sac and the readiness with which it undergoes a form of gangrene. It is clear that, in the case of an infant, causes are at work which tend to bring the skin into a condition which powerfully conduces to the occurrence of local death.

The actual contents of a spina bifida are cerebro-spinal fluid only. This is at once recognised if the cyst is tapped for surgical objects, but it may also become manifest owing to a leakage from the sac when its coverings are very thin and give way from the effects of pressure. In addition to the skin and subcutaneous tissue which cover the sac, there also, generally, runs in the internal surface of the wall a number of nerves which would have emerged from the foramina of the column had the malformed vertebræ been normal. As a rule, these nerves are of small size, but sometimes they are as large as those which go to form the lumbar and the sacral plexuses.

IV. THE PERIPHERAL NERVES

(1) **Atrophy.**—Just as the spinal cord shows evidences of atrophy whenever a part has been amputated or has become useless, so one finds evidences in the peripheral nerves themselves that supply the affected part. In many instances the nerve changes are secondary to the changes in the cord, and this is particularly the case in acute and chronic anterior poliomyelitis. In those conditions the anterior roots and the nerves supplying the affected muscles are definitely smaller than normal. In some instances the spinal portion of the nervous change is not easily recognised. Thus, in hemiatrophy of the tongue, it is not uncommon to find the muscular atrophy and the changes in the corresponding hypoglossal nerve the only recognisable lesions.

The microscopic changes which occur in an atrophied nerve consist in a disappearance of the axis cylinders themselves, combined with an increase in the amount of fibrous tissue which constitutes the neurilemma. It is possible for the amount of newly formed fibrous tissue to fully compensate in bulk for the amount of nerve tissue that has disappeared, and therefore the nerve may not appear to be modified until recourse has been had to the microscope. It will then, however, be found, without doubt, that the actual number of medullated fibres has undergone diminution, while the fibrous tissue between the individual bundles is in obvious excess. In the majority of cases the fibrous tissue is of the fully formed variety, and presents a small number only of nuclei. The nuclei, too, are small and contracted, while they are present in larger number than normal in the interior of

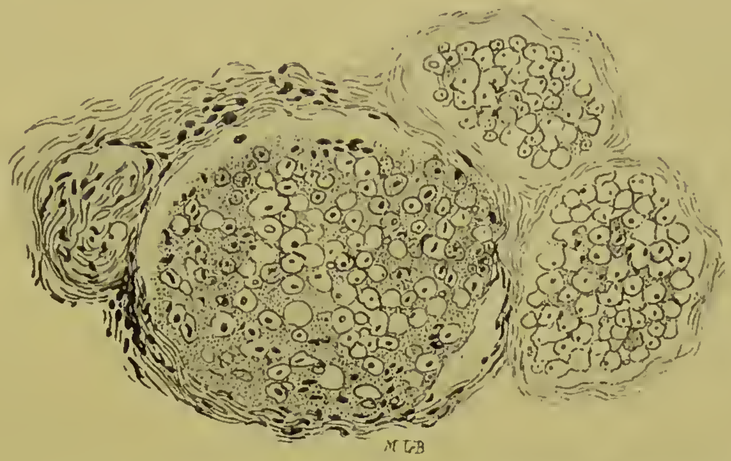

FIG. 168.—SECTION OF HYPOGLOSSAL NERVE FROM A CASE OF HEMIATROPHY OF THE TONGUE. × 60.

Sound side showing normal nerve bundles. Compare with fig. 169.

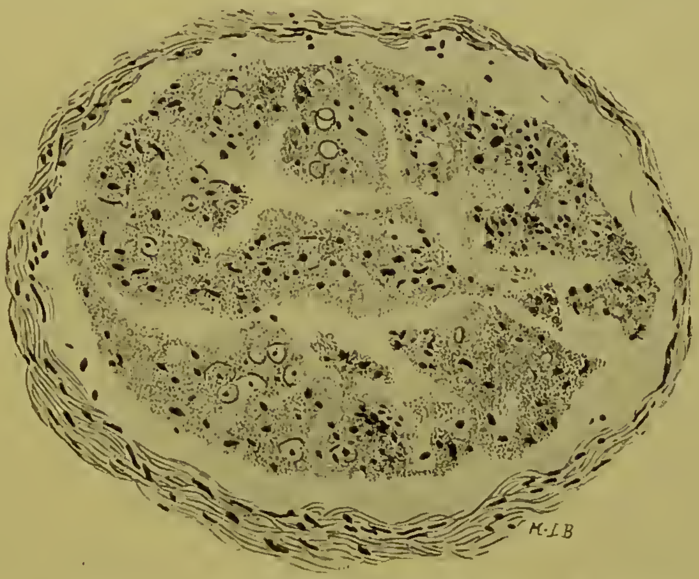

FIG. 169.—SECTION OF HYPOGLOSSAL NERVE FROM A CASE OF HEMIATROPHY OF THE TONGUE. × 60.

Bundle from nerve supplying atrophied side. The bulk of the bundle consists of fibrous tissue with well-marked connective-tissue cell nuclei. A few more or less degenerated nerve sheaths and axis cylinders are seen. Compare with fig. 168.

the bundles. It is quite rare to find that the fibrous tissue has the characters that we have learned to associate with its recent formation.

(2) **Degeneration.**—In speaking of the degeneration of nerve, it must be remembered that the term in reference to nerve has not the same meaning as when applied to the various processes that are grouped together under that name in reference to other tissues. It is true that we find that fatty degeneration is the principal change at work, but the lardaceous, pigmentary, cloudy, mucous, and colloid changes are certainly not to be understood, for it is doubtful whether any of them actually attacks nerve.

In degeneration of nerve the first change affects the medullated sheath in those nerves which are provided therewith. This sheath loses its normal regular shape and rapidly becomes irregular and nodulated. At first the nodosities are separated from one another and the nerve has a beaded outline. This is particularly noticeable in longitudinal sections of nerve or spinal cord which has been stained by Marchi's method and in which some of the nerve fibrils have undergone degeneration and have been taken at a sufficiently early date. Later, the medullated sheath disappears altogether owing to the absorption of the fat droplets which have formed from its disintegration. By this time changes have appeared in the nerve fibrils themselves. Instead of running a direct course throughout the nerve, they become sinuous and wavy, and may in some instances become broken off and their ends curled up. Ultimately they too become broken up and in large measure removed.

At the same time the fibrous-tissue cells of the neurilemma have been undergoing proliferation and have been forming new fibrous tissue. At first the cells do not penetrate within the medullated sheath, but later they invade it, and it is probable that they play a large share in the removal of the drops of fat into which the medullary substance breaks up. Ultimately the entire nerve may be converted into a fibrous cord.

These degenerative changes may affect all the fibres of a mixed nerve, but in that case it is necessary that the process which induces the degeneration shall be at work around the nerve close to the point at which the degenerative changes are taking place. It is clear that although degenerative changes will occur in the efferent nerve fibrils of a mixed nerve when their dominating ganglion cells in the cord have, for some reason, been destroyed, the degenerative changes will not affect the afferent fibrils which run in the same trunk. On the other hand, in tabes dorsalis we have a disease which affects almost exclusively the afferent nerves and leaves the efferent fibrils untouched till much later.

What has been said in the preceding paragraph is quite consonant with the facts that are known as to the degeneration of nerve fibrils when the nerve has been divided experimentally. Examples of this condition are often met with in surgery. Thus we may find the median nerve cut through at the wrist, and in every amputation of a limb mixed nerves are severed. In an uncomplicated case the degeneration proceeds upwards and involves the posterior root ganglia and perhaps the posterior columns of the cord in the case of the afferent fibrils, whereas in the case of the efferent fibrils it stops short at the node of Ranvier next above the seat of injury or a very little higher. Any changes which are found at a later date in the motor portions of the cord or in the anterior roots are dependent upon a disuse atrophy of the kind that has so often come under our notice.

(3) **Inflammation.**—Neuritis is one of the most important of the morbid processes affecting nerves. It may start as a primary condition, as in the case of alcoholic neuritis or diphtheritic neuritis ; or it may commence in the surrounding tissues and extend to the nerve trunks themselves subsequently. It may also be brought about by chemical substances or by bacteria, in the latter instance the irritant being either the toxins formed by bacteria, apart from the bacteria themselves, or bacteria and toxins combined. Of these different classes of irritant we have several specific examples. Thus the neuritis that arises in the course of poisoning by lead or arsenic is definitely produced by a chemical poison. Diphtheria is a marked example of a neuritis caused by the action of a toxin alone, for it has been shown experimentally that neuritis follows repeated injections of diphtheria toxin alone. And the diseases beri-beri and leprosy are evidence that the neuritis may be definitely associated with the presence of micro-organisms in the sheaths of the affected nerve.

Some of the irritants mentioned above seem to have especial tendencies to pick out definite nerves or groups of nerves. Thus alcohol shows a great tendency to affect the muscles of the forearms and legs with the production of much wasting and inability to exert the extensor groups of muscles. Lead, too, shows a tendency to affect the extensor muscles of the forearms, with the production of the condition known as ‘drop-wrist.’ A still more curious feature of poisoning by lead is that the nerve supplying the supinator longus muscle almost always escapes.

It is important to note that a neuritis due to extension of inflammation in the tissues surrounding a nerve-trunk is not of common occurrence. In the case of a psoas abscess, for example, the entire lumbar plexus of nerves may be cleanly dissected out, and yet the functions of the nerves may be carried on perfectly, and the nerves themselves may show no evidences of inflammation to the end. The explanation of this seems to be that the perineurium interposes a barrier between the lymph spaces of the nerve trunk itself and those of the tissues outside. If the perineurium becomes injured in any way, however, extension of the inflammation to the trunk of the nerve itself readily takes place. Nerves, before their exit from the skull or the vertebral canal, do not show this characteristic, and readily become involved. This is well shown in cases of simple or of tuberculous leptomeningitis.

It need hardly be said that neuritis is associated with a number of other changes than those occurring in the nerve itself. Impairment of movement and of sensation, with subsequent nutritive changes in the muscles and the skin, is certain to occur in a greater or less degree. The degenerative processes occurring in the nerve as a consequence of the inflammation may also extend to the posterior root ganglia and the posterior columns of the cord. Extension to the anterior and lateral columns is not likely to occur, but the inflammatory process may lead to a leptomeningitis and subsequently to a myelitis.

In the case of tabes dorsalis and certain other chronic diseases of a similar kind, the association of degenerative changes in the cord with degenerative changes in the peripheral nerves is constant, although the degrees to which the two parts of the nervous system are affected are not always the same. In the case of such a disease as acute anterior poliomyelitis it is clear that the amount of degeneration which is found in the nerves depends entirely upon the degree to which the anterior cornual cells have suffered.

(4) **New-growths.**—Tumours of nerves are very uncommon. The commonest is that which is termed the **amputation neuroma**. It is chiefly found to affect the terminal end of the sciatic nerve in cases in which the lower limb has been amputated. The end of the nerve is found to be bulbous, and it may be as large as a pigeon's egg. On making a section, it is seen to consist of a dense mass of coiled-up fibres, so that it has a very close macroscopic resemblance to the section of a fibromyoma. Microscopically the tumour shows the presence of large numbers of convoluted and contorted nerve bundles, with the addition of a large amount of fibrous tissue. Stained by the Weigert-Pal method, it is abundantly clear that there has been a new formation of nerve matter. This may

have arisen because division has taken place of the fibres that were formerly present in the end of the nerve, or because the axis cylinders have elongated and have become coiled up in a terminal mass of inflammatory fibrous tissue, or both of these processes may have been at work. In any case, it is certain that we have here to do with a definite tumour in the composition of which nervous material plays an essential part.

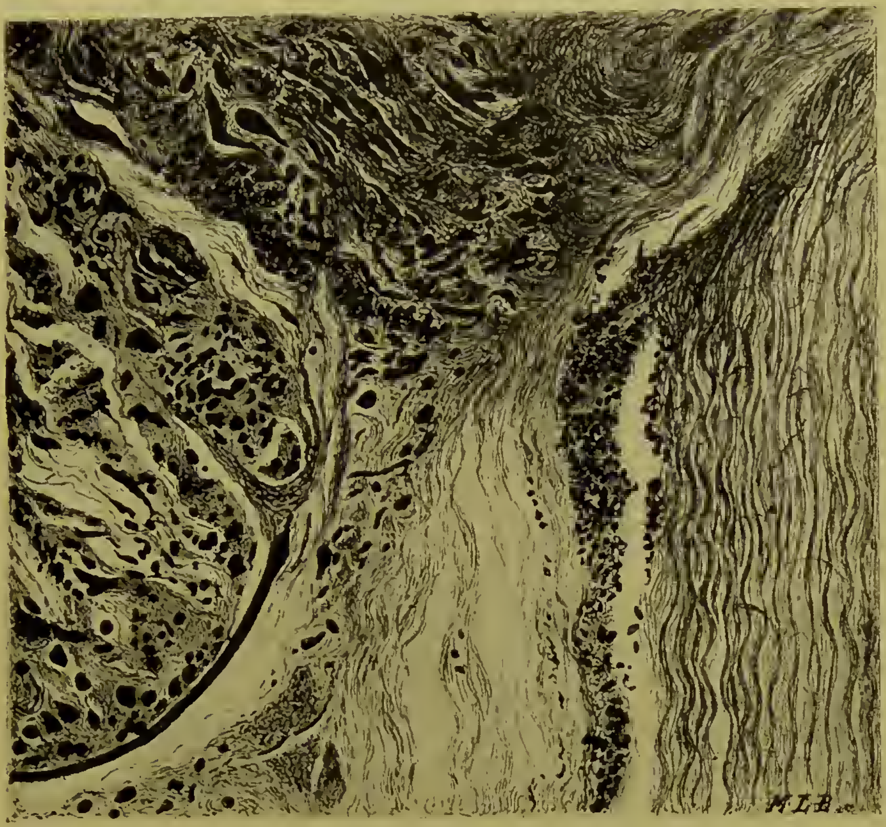

FIG. 170.—SECTION OF AMPUTATION NEUROMA. × 60.

Numerous contorted and irregular nerve fibres, partly isolated, partly in bundles, are seen cut in all directions. They are stained black by Pal's modification of Weigert's method. To the right of the figure is a bundle of nerve fibres cut longitudinally and having a fairly normal appearance. Between the nerve fibres is dense fibrous tissue.

In the large majority of cases, however, tumours of nerves are rather tumours *on* nerves. Sufficient reference has already been made to the fact that such tumours are almost always fibromata, and mention has been made of 'Recklinghausen's disease,' in which their presence is characteristic.

Sarcomata of nerves are excessively rare, but they may occur as a terminal change, as was the case in the specimen which is figured. Here it is almost certain that the sarcoma which involved the left vagus had originated in some of the 'neuromata' similar to those which are seen to be present along the course of the right vagus. The specimen figured came from a case of Recklinghausen's disease, and minute tumours were present on a large number of small nerves in the mesentery and abdominal cavity generally.

Carcinoma does not affect nerves primarily, nor is it at all common to find secondary nodules of carcinoma in nerves. It is, of course, common for nerves to be involved in a mass of carcinoma, but then it is general for the nerve to pass through the mass unaffected by actual growth into its tissue. In the case of the small nerve trunks it is probable that atrophy from pressure takes place. It is impossible to doubt that this occurs in a case of carcinoma of the breast, for example, to some degree.

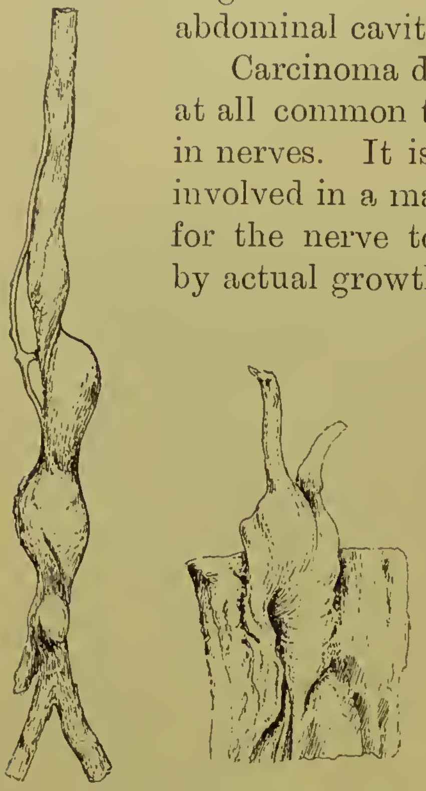

Fig. 171.—Vagus Nerves from Case of Recklinghausen's Disease. × $\frac{2}{3}$.

The right nerve simply shows bulbous enlargements; the left, which it was impossible to dissect out owing to the presence of masses of sarcomatous tissue, ended in a mass of spindle-cell sarcoma, a square portion of which is shown. From a specimen in the St. George's Hospital Museum.

THE SYMPATHETIC SYSTEM

Widely distributed as is that portion of the nervous system which is included under the term 'sympathetic,' little or nothing is known as to the pathological changes which are undergone by the nerves, and very little is known as to the changes which take place in the ganglia.

So far as the ganglia are concerned, the principal change which has been described is fibrosis. This has been found to affect the cervical ganglia in cases of exophthalmic goitre, and the solar plexus in cases of diabetes mellitus and Addison's disease. That there is sometimes to be found in the parts mentioned a condition which we are accustomed to speak of as a chronic fibrosis or sclerosis, there is no doubt. But how far the change is competent to explain the diseases in question, if at all, is very uncertain. It is therefore unnecessary to pursue the matter further here. The only affection of the sympathetic nerves themselves which need be mentioned is the presence on them of multiple 'neuromata' in Recklinghausen's disease.

INDEX

- Abortion, 609
- Abscess, 67
  - and pressure atrophy, 71
  - bacteria in, 68
  - method of formation, 69
  - of bone, repair of, 100
  - of kidney, 543
  - of liver, around foreign body, 456
    - pyæmic, 456
    - pylephlebitic, 454
    - tropical, 453
  - of lung, 507
  - of pancreas, 478
  - pharyngeal, 383
  - pointing of, 70
- Acidophil leucocytes, 241
- Acromegaly, 348
- Actinomycosis, 116
  - of appendix, 422
  - of bone, 340
  - of liver, 458
  - of lung, 520
- Acute yellow atrophy of liver, 451
- Addison's disease, 568
  - intestine in, 26
  - pigmentation in, 25
- Adenitis, forms of, 325
- Adeno-carcinoma, 156
  - of liver, 467
- Adeno-cystoma of bile ducts, 475
- Adenoids, 382
- Adenoma, structure and varieties of, 179
  - of breast, 614
  - of intestine, 427
  - of liver, 465
- Adipose heart, 284
- Adrenal bodies, 568
- Agenesia, 7
- Agonal thrombus, 126
- Air embolism of lung, 499
- Albinismus, 25, 626
- Alveolar adenoma, 179
  - sarcoma, 194
- Amitosis, 76
- Ampulla of Vater, 475
- Amputation neuroma, 690
- Amygdalitis, 392
- Amyloid change, 16
- Anæmia, 248
  - spleen in, 319
- Anæmias, blood changes in, 248
  - toxic, 251
  - with leucocytic changes, 251
  - without leucocytic changes, 248
- Anæmic infarct, 32, 133
- Anasarca, 42
- *Anchylostomum duodenale*, 433
- Aneurysm, 300
  - cirsoid, 310
  - dissecting, 303
  - false, 304
  - fusiform, 301
  - of cardiac valves, 272
  - of cerebral artery, 672
  - of heart, acute, 282
    - chronic, 288
  - saccular, 301
  - traumatic, 304
- Aneurysmal varix, 169
- Angeioma, 147, 169
  - of liver, 465
- Angeio-sarcoma, 203
- Angina pectoris, 286
- Angular curvature of spine, 338
- Anthracosis, 27
- Anthrax, 631
- Antrum, 391
- Aorta in chlorosis, 8
- Aplasia, 7
- Apoplexy, cerebral, 672
  - pulmonary, 135, 498
- Appendicitis, 420
- Argyriasis, 27
- Arterial congestion, 39
  - thrombosis, 129
- Arteries, 295
  - degeneration of, 296
  - hypoplasia and atrophy of, 295
  - new-growths of, 309
- Arterio-sclerosis, 306
- Arteritis, 307
  - deformans, 300
- Arthritis deformans, 366
- Arthroses, chronic, 366
- *Ascaris lumbricoides*, 433
- Ascites, 42
  - chylous, 316
- Atelectasis, 491
- Atheroma, 296
  - and caseation, 34

- Atheroma of cerebral vessels, 671
- Atheromatous ulcer, 299
- Atresia ani, 410
- Atrophy, 5
  - and abscess, 71
  - and fibrosis, 8
  - and venous congestion, 37
  - causes of, 9
  - of arteries, 295
  - of heart, brown, 26
  - of intestines, 409
  - of kidney, 530
  - of muscles, 370
  - of ovaries, 598
  - of peripheral nerves, 686
  - of spinal cord, 675
  - of thyroid, 527
  - of uterus, 587
  - optic, 643
  - serous, of myocardium, 283
- Atypia in carcinoma, 219
- Auricle of ear, diseases of, 645

- Bacilli, 56
  - in inflammation, 56
- Bacilluria, 566
- Bacteria, 563
  - in suppuration, 68
  - in urine, 566
  - pathogenetic, 57
- Bacterial toxins, 58
- Balanitis, 570
- 'Ball clots' in heart, 279
- artholin's glands, 585
- asophil leucocytes, 241
- Bedsores, 634
  - acute, 31
- Bile passages, 470
  - pigment in kidney, 531
- *Bilharzia hæmatobia*, ova of, in urine, 566
- Biliary cirrhosis, 463
- Biurate of sodium in gout, 360
- Blisters, 634
- Blood, 235
  - basophil leucocytes, 244
  - changes in anæmia, 248
  - corpuscles, red, 235
    - white, 240
  - degenerated cells of, 239
  - hyaline cells, 243
  - lymphocytes, 243
  - megalocytes, 237
  - microcytes, 237
  - myelocytes, 245
  - nucleated red cells, 238
  - oxyphil leucocytes, 241
  - platelets, 256
- Blood-vessels, 295
  - regeneration of, 84
- Boils, 630
- Bone, abscess of, repair of, 100
  - atrophy of, 329
  - deformities due to, 349
- Bone, degenerative changes in, 329
  - inflammation of, 332
  - new-growths of, 351
  - regeneration of, 80
  - repair after simple fracture, 93
  - sarcomata of, 352
  - sclerosis of, 101
  - secondary carcinoma of, 355
  - syphilitic disease of, 334
  - tuberculous disease of, 337
- *Bothriocephalus latus*, 433
- 'Bow' legs, 344
- Brain, affections of cerebral vessels, 669, 671
  - atrophy and hypertrophy, 662
  - carcinoma, 668
  - cerebral abscess, 663
  - embolism, 669
  - endothelioma, 667
  - glioma, 667
  - inflammation of, 663
  - in old age, 8
  - new-growths in, 667
  - pigmentation, 661
  - red and white softening, 659
  - retrogressive changes, 659
  - rupture, 671
  - sarcoma, 668
  - syphilis, 666
  - syphilitic endarteritis, 670
  - thrombosis, 670
  - tuberculosis, 665
- Brain-sand, 194
- Breast. (*See* Mammary gland)
- Bronchial tubes, 488
- Bronchiectasis, 490
- Broncho-pneumonia, 502
- Brown atrophy, 26
  - induration, 496
- Bunion, 375
- Burns, 633
- Bursæ, 375
- 'Butter-cysts,' 620
- 'Buttressing' of bone, 344

- Calcification, 22
  - blood supply and, 22
  - in uterine fibroid, 23
  - of cartilage, 357
  - of laryngeal cartilages, 481
- Calcifying sarcoma, 197
- Calculi, biliary, 470
  - intestinal, 432
  - pancreatic, 480
  - prostatic, 583
  - salivary, 394
  - tonsillar, 394
  - urinary, 562
- Calculous pyelitis, 553
- Callosity, 146, 157
- Callus, 94
- Canalisation of thrombi, 131
- Cancellous exostoses, 168
- Cancer en cuirasse, 619

Cancerous cirrhosis of liver, 466
Cancrum oris, 380
Capillaries, 314
Capillary nævi, 170
Capsular cataract, 641
Carbuncle, 630
Carcinoma, 207
  colloid, 19, 224
  columnar-cell, 215
  duct, 218
  lymphatics in, 317
  of bone, secondary, 355
  of brain, 668
  of breast, 617
  of gall-bladder, 474
  of intestine, 428
  of larynx, 487
  of liver, 466
  of pancreas, 479
  of uterus, 594
  rodent, 212
  sarcomatodes, 207
  spheroidal-cell, 219
  squamous-cell, 208
  villous, 218
Cardiac thrombi, 278
Caries, 72. (*See* Osteitis)
Carnification, 494
Cartilage, 357
Caseation, 32
  in syphilis, 111
  in tuberculosis, 107
Caseous tuberculosis of lung, 515
Casts in urine, 565
Cataract, 640
Catarrhal inflammation, 64
Cauliflower growths, 210, 595
Cavernous lymphangeioma, 172
  nævi, 171
'Cell nests,' 211
Cells, epithelioid, 106
  giant, 98
  lymphoid, 106
Cellular changes in inflammation, 48
Central canal of spinal cord, diseases of, 684
Cerebral abscess, 663
  apoplexy, 672
  embolism, 669
  thrombosis, 670
  vessels, affections of, 669
Cerebro-spinal meningitis, 652
'Chalk stones,' 361
Chancre, hard or Hunterian, 110
Charcot's disease of joints, 369
Chemiotaxis, 50
Chloroma, 26, 193
Chlorosis, aorta in, 8
'Choked disc,' 643
Cholecystitis, 473
Cholera asiatica, 415
Chondritis, 357
Chondroma, 352
Chondro-sarcoma, 196
Chorion, 607
Choroid, 640
Chronic fibroses, 121
Chylous ascites, 316
Chyluria, 316, 564
Cicatrix, 92
Ciliary body, 640
Cirrhoses of liver, 458
  intercellular, 464
  multilobular or atrophic, 459
  unilobular or hypertrophic, 462
Cirsoid aneurysm, 310
'Clergyman's throat,' 482
Cloacæ, 101
Cloudy swelling, 14
  of kidney, 531
  of myocardium, 286
Coagulative necrosis, 31
Cocci, pyogenetic, 68
Cohnheim, theory of tumour formation, 141
Colitis, membranous, 415
  ulcerative, 422
Collapse of lung, 492
Colliquative necrosis, 32
Colloid carcinoma, 224
  change, 19
Colpitis, 586
Columnar-cell carcinoma, 215
Condylomata, 112
Congenital cystic disease of kidney, 561
    of liver, 469
  malformations of the heart, 292
  syphilis, 114
Congestion, 36
  arterial, 39
  capillary, 314
  hypostatic, 40
  venous, 37
Conjunctivitis, 637
Connective tissue, regeneration of, 78
  tumours of, malignant, 186
    non-malignant, 161
Consecutive nephritis, 541
Contracted granular kidney, 546
  white kidney, 539
Cornea, diseases of, 638
Corns, 158
'Corns' on pericardium, 264
Corpora lutea, 599
Corpuscles. (*See* Blood)
Corrosive poisons, effects of, on alimentary tract, 406
Coryza, 64, 377
Cowper's glands, 583
Coxa vara, 351
Craniotabes, 336
Cretinism, 527
Croup, 65
Crystals in urine, 567
Cyclitis, 640
Cylindroma, 203
'Cystadenomata, proliferating,' 155
Cystic disease, congenital, of kidney, 561
    of liver, 469
  lymphangeioma, 172

Cystitis, 555
Cysto-carcinoma of breast, 619
Cystoma, 228
Cysts, 226
  dental, 390
  of liver, 469
  of pancreas, 480

DEAF-MUTISM, 649
Death, local, 28
Deciduoma malignum, 607
Deformities due to the bones, 349
Degeneration, 5. (*See also* under separate organs)
  Maragliano's, 239
Demarcation, line of, 31
Dental cyst, 390
  osteoma, 168
Dermatitis, 628
Dermoid cysts, 231
Diabetes mellitus, and pulmonary tuberculosis, 10
  pancreas in, 478
  wasting in, 10
Dilatation of heart, 289
Diphtheria, 378
  larynx in, 482
Diphtheritic enteritis, 414
  membrane, 32
Diplococci, 57
Dissecting aneurysm, 303
Disseminated sclerosis, 681
Disuse, atrophy from, 9
  fatty degeneration from, 14
Diverticula of œsophagus, 397
Drop-wrist, in lead poisoning, 689
Duct carcinoma, 159, 218, 617
  papilloma, 621
Duodenal ulcer, 416
'Dupuytren's contraction,' 374
Dysentery, 423

EAR, 645
Eburnation, 366
Ecchondroma, 166
Ecchondrosis, 166
Ectropion cervicis, 591
Effusion, pericardial, 259
  fluid in, 42
Elephantiasis, 316
  scroti, 580
  vulvæ, 584
Emaciation, 9
Embolism, 131
  cerebral, 669
  results of, 132
Embryonic remnants, theory of tumour formation, 141
Emphysema, 494
  varieties of, 496
Empyema, 524
'Encephaloid cancer,' 222
Enchondroma, 166
Endarteritis obliterans, 111, 308
  of cerebral vessels, 670
Endocarditis, aneurysm of valves, 272
  non-valvular, 278
  valvular, acute, 266
    chronic, 273
Endometritis, 588
Endosteal sarcoma, 354
Endothelioma, 195, 201
  of brain, 667
  of peritoneum, 441
Enteritis, 414
Enteroliths, 432
Entozoa, 433
Epididymitis, 573
Epispadias, 562
Epithelial pearls, 211
Epithelioid cells, 106
Epithelioma, 208 (footnote)
Epithelium after inflammation, 76
  regeneration of, 76
  transitional, 148
Epulis, 205, 355, 390
Ergotism, 30
Erosion of cervix uteri, 591
Erysipelas, 632
Erythema, 631
Erythroblasts. (*See* Blood corpuscles)
Eschar, 28
Exophthalmic goitre, 528
Exostoses, 168, 351
Explosive cells, 243
External auditory meatus, diseases of, 645
Extra-uterine gestation, 608
Extroversion of bladder, 562
Exudation fluid, 44
Eye, 637
Eyeball, tumours of, 644

FÆCAL ulcers, 425
Fallopian tubes, 595
False aneurysm, 304
  membranes, 31, 44
Farcy, 118
Fasciculation of bladder, 555
Fat embolism, 499
  necrosis, 32
  physiological deposition of, 11
Fatty change, 10
    and cloudy swelling, 15
    and colliquative necrosis, 32
    in heart, 12
    in liver, 12, 448
    in pathological material, 14
  degeneration from disuse, 14
    of kidney, 531
    of myocardium, 284
  infiltration, and pressure atrophy, 14
    of myocardium, 284
Fever, tongue in, 386
Fibrinoid change, 21
  in pleurisy, 523
Fibro-adenoma. (*See* Tumours)

Fibro-adenoma of breast, 147
Fibroid degeneration of heart, 287
  tuberculosis of lung, 519
Fibroma, 161
  lamellar, 440
  molluscum, 635
  recurrent, 139
Fibro-myoma of uterus, 177, 593
Fibroses, the chronic, 121
Fibrosis, 63
  chronic, of myocardium, 287
  of kidney, 546
  of lung, 511
Filariasis, 316
Fissured anus, 426
Fistula in ano, 426
Flattened pelvis, 344
Focal necroses, 450
'Fœtal rickets,' 341
Fœtus, morbid conditions of, 609
Follicular stomatitis, 380
Foramen ovale, patency of, 292
Fracture, repair after simple, 93
Fractures of cartilage, 357
'Friction rub' in pericarditis, 259
'Fulminating' appendicitis, 421
Function, impairment of, in inflammation, 46
Furuncles, 630
Fusiform aneurysm, 301

Galactocele, 620
Gall bladder, 473
  stones, 470
Ganglion, 374
Ganglionic neuroglioma, 174
Gangrene, 28
  of lung, 509
  symmetrical, 30
Gangrenous pancreatitis, 478
  stomatitis, 380
Gastric ulcer, 399
Gastritis, 399
Genu valgum, 351
Giant cells, 98
Giant-cell sarcoma, 190
Giants, 8
Gland, regeneration of, 83
Glanders, 118
Glandular tissue, non-malignant tumours of, 179
Glaucoma, 640
Glioma, 173
  of brain, 667
  of eye, 644
Glomerular nephritis, 536
Glossitis, 388
Glossy skin, 623
Glüge's corpuscles, 660
Goitre, 528
Gonorrhœa, 558
Gonorrhœal rheumatism, 362
Grafting of skin, 77
Granular conjunctivitis, 638
Granular pharyngitis, 381
Granulation loops, 86, 97
  tissue, 95
'Granulations' in endocarditis, 267
Granulomata, infective, 105
Growth-liberation theory of tumour formation, 145
Gout, 360
Gumma, 112
  of liver, 457
  of spinal cord, 679
  of testis, 576
Gums and teeth, 389

'Habit of growth' theory of tumour formation, 145
Hæmangeioma, 169
Hæmangeiosarcoma, 203
Hæmatocele, 579
Hæmatoidin, 24, 25
Hæmatoma, 227
  auris, 645
Hæmatometra, 603
Hæmatosalpinx, 597
Hæmolysis and hæmosiderin, 24
Hæmo-pericardium, 260
Hæmophilia, capillaries in, 314
Hæmorrhagic infarct, 134
Hæmorrhoids, 312
Hæmosiderin, 24
'Hardbake' spleen, 319
Heart, brown atrophy of, 26
  congenital malformations of, 292
  dilatation and hypertrophy, 289
  fatty change in, 12
Hepatisation of lung, 499
Hepatitis, acute, 453
Hernia, 411
  testis, 574
Heterologous tumours, 137
Histioid tumours, 136
'Hobnail' liver, 459
Hodgkin's disease, 254
Homologous tumours, 137
'Horseshoe' kidney, 560
'Hour-glass' contraction, 402
'Housemaid's knee,' 376
Hunterian chancre, 110
Hyaline cells of blood, 243
  change, 21
  in myocardium, 287
Hydatid cysts of liver, 469
Hydatidiform mole, 607
Hydrocele, 579
Hydrocephalus, 42, 662
  in posterior basic meningitis, 654
Hydromyelia, 685
Hydronephrosis, 552
Hydro-pericardium, 62, 260
Hydrops folliculi, 600
Hydrosalpinx, 597
Hydrothorax, 42
Hygroma, cystic, 173, 317
Hyperæmia, 36. (*See* Congestion)

Hyperostosis, 167
Hyperplasia, 6
Hyperpyrexia and hyperthermia, Nissl's bodies in, 683
Hypertrichosis, 625
Hypertrophy, 5
    of heart, 289
    of uterus, 587
Hypoplasia, 7
    of arteries, 295
Hypospadias, 559
Hypostatic congestion, 40
    congestion of lung, 497
    pneumonia, 502

Implantation cysts, 233
Indigestion, 398
Infantile paralysis, 682
Infarct, 133
    simple, and coagulative necrosis, 31
Infarction, 133
    hæmorrhagic, of lung, 498
    of kidney, 534
    of liver, 445
    of spleen, 321
Infective granulomata, 105
    inflammation, 60
Infiltrations, 5
Inflamed hernia, 412
Inflammation, 35
    abscess in, 67
    and regeneration, 76
    bacteria in, 56
    cardinal signs of, 35
    causes of, 56
    cellular changes in, 48
    chemotaxis in, 50
    congestion in, 36
    connective tissue after, 78
    fixed tissue cells in, 55
    impairment of function in, 46
    migration of leucocytes in, 49
    œdema in, 42
    pain in, 45
    parasites and, 59
    phagocytosis in, 51
    pus in, 53
    repair after, 89
    resolution in, 66
    sequels of, 66
    suppuration in, 67
    temperature in, 45
    types of, 59
    ulceration in, 67
Inhalation pneumonia, 506
'Insane ear,' 645
Insular sclerosis, cord in, 681
Internal ear, diseases of, 648
Interstitial inflammation, 63
Intestines, 409
    abnormal contents of, 430
    atrophy of, 409
    corrosive poisoning, 407
Intestines, inflammation of, 413
    malformations and malpositions, 410
    new-growths of, 427
    parasites, 433
    pigmentation of, 26, 409
    syphilitic ulceration of, 425
    tuberculous ulcer of, 418
Intra-alveolar hæmorrhages, 498
Intra-hepatic gall-stones, 471
Intussusception, 412
Involucrum, 101
Iris, 639
Iron in pigmentary changes, 24, 449, 531
Ivory exostosis, 168, 351

Jaundice, pigments in, 25
Joints, 358
    acute inflammations, 358
    chronic inflammations, 363
    loose bodies in, 369
    pyæmic inflammations, 362

Karyokinesis, 76
Keratitis, 639
Keratoma, 158
Kidneys, 530
    atrophy and hypertrophy, 530
    chronic fibrosis, 546
    degenerations and infiltrations, 530
    inflammations, 536. (*See* Nephritis)
    new-growths, 549
    vascular changes (non-inflammatory), 533
Knock-knee, 351

Labial abscess, 585
Lamellar fibroma, 440
Lardacein, 16
Lardaceous change, 16
    in kidney, 532
    in liver, 447
    in myocardium, 287
    in spleen, 16
Laryngeal cartilages, calcification of, 481
Larynx and trachea, 481
Lateral sclerosis, cord in, 681
Leiomyoma, 176
    of uterus, 593
Lens, 640
Leontiasis ossea, 349
Leprosy, 119
    of larynx, 484
Leptomeningitis, 650
Leuchæmia, 251
Leucoblast, 253
Leucocytes, 240
    in phagocytosis, 52
    migration of, in inflammation, 49

Leucocytes, varieties of, 241
Leucocythæmia, 252
  liver in, 452
  spleen in, 319
Leucocytosis, 246
Leucoderma, 626
Leucopenia, 247
Leucoplakia, 388
Line of demarcation, 31
'Lipping' of bone, 367
Lipoma, 11, 165
'Lipoma nasi,' 626
Lipomatosis, 10
Lips, 385
  carcinoma of, 385
  macrocheilia, 386
Lithopædion, 23, 609
Liver, 443
  acute yellow atrophy, 451
  chronic fibroses, 458
  degenerations and infiltrations, 446
  fatty changes, 448
  focal necrosis, 450
  in chronic venous congestion, 37
  in congenital syphilis, 114
  inflammations of, 453
  lardaceous change, 447
  leuchæmia, 452
  new-growths, 465
  nutmeg, 38
  siderosis, 449
  vacuolation, 450
  vascular changes, non-inflammatory, 443
Local death, 28
Locomotor ataxy, cord in, 681
Loose bodies in joints, 369
Lungs, diseases of, 491
Lupus, 105, 632
Lymphadenitis, 323
Lymphadenoma, 183, 254
Lymphangeiectasis, 172, 316
Lymphangeioma, 169, 317
  cavernous, 172
  cystic, 172
Lymphangeio-sarcoma, 203
Lymphangeitis, 316
Lymphatic glands, 323
Lymphatic leuchæmia, 252
Lymphatics, in carcinoma, 317
  in œdema, 315
  regeneration of, 86
Lymph channels, 315
Lymphocythæmia, 253
Lymphocytes, 243, 106
Lymphoma, 183
Lympho-sarcoma, 199

MACROCHEILIA, 172, 386
Macroglossia, 172, 388
Maculæ, 629
Madura foot, 117, 340
Malaria, spleen in, 319
Malformations of generative organs, 559, 603
  of heart, 292
  of intestine, 410
  of lungs, 491
  of urinary apparatus, 559
Malignancy, criteria of, 138
Malignant disease, emaciation in, 10
  pustule, 631
  tumours, 186
  ulcers, 74
Mammary gland, 611
Maragliano's degeneration, 239
'Masked iron,' 24
Mastitis, 612
'Mastzellen,' 244
Meckel's diverticulum, 410
Megaloblasts, 239
Megalocytes, 237
Melæna, 430
Melanin, 26, 193
Melanotic sarcoma, 192
  pigment in, 25
Melanuria, 193
Melon-seed bodies, 375
Membrane, pyogenic, 70
Membranous colitis, 415
  croup, 65
Menière's disease, 648
Meningeal hæmorrhage, 657
Meningitis, cerebro-spinal, 652
  posterior basic, 653
  spinal, 677
  suppurative, 651
  tuberculous, 655
Menorrhagia, 588
Metaplasia, theory of, 153
Metritis, 588
Metrorrhagia, 588
Micrococci, 57
Microcytes, 237
Middle ear, diseases of, 643
Midgets, 8
Migration of leucocytes, 49
Miliaria, 630
Miliary tubercle, 105
  tuberculosis of lung, 515
'Milk spots,' 264
Mitosis, 76
Mixed-cell sarcoma, 190
Molecular necrosis, 151
Molluscum fibrosum, 162
Mouth and naso-pharynx, diseases of, 377
  in corrosive poisoning, 406
Mucin, 18
Mucous polypus, 164
Mucus, 18, 19
'Mulberry' calculus, 563
Multiple sclerosis, cord in, 681
Mummification, 28
Mumps, 394
Muscles, 370
  animal parasites in, 373
  atrophy of, 370
  inflammation of, 371

Muscles, in phthisis, 10
  new-growths of, 372
  regeneration of, 82
Muscular tissue, non-malignant tumours of, 174
Myelitis, 675
Myelocytes, 245
Myeloid sarcoma, 190
Myeloma, 190
Myocarditis, pyæmic, 282
  simple, 280
  syphilitic, 282
  tuberculous, 283
Myocardium, 280
  brown atrophy of, 26
  chronic fibrosis of, 287
  cloudy swelling of, 286
  hypertrophy of, 289
  new-growths of, 292
  retrogressive changes, 283
  serous atrophy of, 283
  ‘ tabby-cat striation,’ 284
Myositis, 371
  ossificans, 81, 169, 372
Myxœdema, 527
Myxoma, 162

Nævus, 169
Nasal polypi, 394
Necrosis, coagulative, 31
  colliquative, 32
  fat, 32
  molecular, 72
Nematode worms, 433
Neoplasms, 136. (*See* New-growths, and Tumours)
Nephritis, 536
  consecutive, 541
  glomerular, 536
  pyonephrosis, 543
  tubal (*q.v.*), 536
  tuberculous, 544
Nerve tissue, regeneration of, 87
Nervous control, atrophy from removal of, 9
  tissue, non-malignant tumours of, 178
Neuritis, optic, 642
  peripheral, 689
Neuro-glioma, ganglionic, 174
Neuro-retinitis, 642
Neuroma, 178
New-growths, 136. (*See also* Tumours)
  changes undergone by, 150
  classification of, 152
  effects on surrounding tissues, 149
  general histology of, 146
  molecular necrosis of, 151
  of adrenals, 569
  of arteries, 309
  of bladder, 556
  of bone, 351
  of brain, 667
  of breast, 614
New-growths of capillaries, 314
  of eyeball, 644
  of intestine, 427
  of kidney, 549
  of larynx and trachea, 486
  of liver, 465
  of lung, 521
  of muscles, 372
  of myocardium, 292
  of nerves, 690
  of ovary, 600
  of pancreas, 479
  of penis, 571
  of peritoneum, 441
  of prostate, 581
  of salivary glands, 394
  of skin, 635
  of spinal cord, 679
  of testis, 576
  of thyroid, 529
  of tongue, 389
  of tonsils. 393
  of uterus, 593
  of veins, 313
Nipple, diseases of, 622
Nissl bodies, 683
Nodes, 334
Noma, 380
  vulvæ, 584
Non-malignant tumours, 157
Normoblasts, 239
Nose, chronic specific inflammations of, 383
‘ Nutmeg ’ liver, 443

Oat-cell sarcoma, 190
Obesity, 10
Odontoma, 168, 390
Œdema, 42
  causes of, 43
  fluid in, 43
  lymphatics in, 315
  of larynx, 482
  of lung, 498
  of scrotum, 580
  of skin, 626
Œdematous fibromata, 163
Œsophagus, 395
  carcinoma of, 395
  idiopathic dilatation and hypertrophy of, 398
  in corrosive poisoning, 406
  pouching of, 397
  sarcoma of, 397
  stenosis of, 10, 397
  varicose veins of, 398
Oïdium albicans, 379
Oligochromæmia, 236
Oligocythæmia, 236
Omphalo-mesenteric duct, 410
Oöphoritis, 598
Ophthalmia, sympathetic, 644
Optic atrophy, 643
  neuritis, 642

Orchitis, 573
Organisation of thrombus, 130
Organoid tumours, 136
Osteitis, 332
    deformans, 346
Osteoclasts, 329
Osteoid sarcoma, 198
Osteoma, 167, 351
Osteomalacia, 330
Osteophytes, 168, 351
Osteo-sarcoma, 198
Osteoses, chronic, 346
Otitis media, 647
Otorrhœa, 647
Ovarian cysts, paramucin in, 18
Ovaries, 598
Ovulæ Nabothi, 591
Oxyphil leucocytes, 241
Oxyuris vermicularis, 433
Ozæna, 384

PACHYMENINGITIS hæmorrhagica, 658
Paget's eczema, 622
Pain in inflammation, 45
Pancreas, diseases of, 478
    in fat necrosis, 32
Pannus, 638
Papillary adenoma, 179
    cystadenoma of kidney, 551
Papilliferous ovarian cysts, 602
Papilloma, 157
    of larynx, 487
    of penis, 571
Papules, 629
Paralytic congestion, 39
Paramucin, 18
Paraphimosis, 571
Parasites as irritants, 59
Parasitic theory of tumour formation, 142
Parenchymatous inflammation, 63
    nephritis, 536
'Parotid tumours,' 394
Parovarian cysts, 227, 601
Parrot's bossing, 336
Parturition, pathological phenomena of, 604
Patency of foramen ovale, 292
Pathogenetic bacteria, 57
Pearls, epithelial, 211
Pelvis of kidney, 552
Penis, 570
Perforating ulcers, 635
Peri-arteritis nodosa, 309
Peribronchitis, 489
Pericardial effusion, 259
Pericarditis, acute, 257
    chronic, 263
    dry, 259
    fibrinous, 259
    hæmorrhagic, 259
    suppurative, 265
    tuberculous, 264
Pericardium 257
Pericardium, adherent, 263
    'milk spots,' 264
Perichondritis, 357
Periosteal sarcoma, 352
Peripheral nerves, diseases of, 686
    neuritis, 689
Peritoneum, 434
    inflammation of, 434
    new-growths of, 441
Peritonitis, acute, 435
    chronic, 439
    tuberculous, 437
Perityphlitic abscess, 421
Pernicious anæmia, 237
    hæmosiderin in, 24
Petechiæ, 628
Phagèdæna of penis, 571
    vulvæ, 584
Phagocytosis, 51
Pharyngeal abscess, 383
Pharyngitis, granular, 381
Phimosis, 570
Phlebitis, 312
Phlebolith, 312
Phlegmasia dolens, 129
Phthisis, muscles in, 10
Physiological deposition of fat, 11
Pigments, extrinsic, 26
    intrinsic, 24
Pigmentary changes, 24
    in intestines, 409
    in kidney, 531
    'masked iron' in, 24
Pigmentation in Addison's disease, 25
    of brain, 661
    of skin, 626
Piles, 312
Placenta, morbid conditions of, 606
Plastic bronchitis, 489
Platelets, blood, 256
Pleura, repair after inflammation, 102
Pleuræ and pleural cavities, 522
Plexiform neuroma, 179
Pneumokonioses, 513
Pneumonia, hypostatic, 502
    inhalation, 506
    lobar, 499
    lobular, 502
Poikilocytosis, 238
Pointing of abscess, 70
Poliomyelitis, 682
Polymorphonuclear leucocyte, 241
Polypi, 161, 183
    intestinal, 427
    nasal, 384
Pons Varolii, hæmorrhages into, 674
Posterior basic meningitis, 653
Posthitis, 570
Pott's curvature of spine, 338
Pressure atrophy, 9
    from fatty infiltration, 14
Progressive muscular atrophy, 370, 682
Proliferating cyst-adenomata, 155, 217
Prostate gland, diseases of, 581
Psammoma, 193

Pseudo-hypertrophic muscular paralysis, 8, 371
Pseudo-hypertrophy, 8
Pseudo-leuchæmia, 254
    kidney in, 535
Pseudo-tuberculosis, 520
Psorosperms, 143
Puerperal fever, 605
Pulmonary apoplexy, 135, 498
    tuberculosis, 514
        and diabetes mellitus, 10
        and lardaceous change, 17
Purpura, cutaneous hæmorrhages in, 628
Pus, 53
    cells in, 54
    liquor puris, 54
    in urine, 564
    origin of cells in, 54
Pustules, 630
Pyæmic abscess of kidney, 543
    of liver, 456
    of lung, 509
    of myocardium, 282
    of spleen, 321
Pyelitis, 553
Pylephlebitis, 454
    of joints, 362
Pyogenetic cocci, 68
'Pyogenic membrane,' 70
Pyonephrosis, 543
Pyopneumothorax ,5 4
Pyosalpinx, 597

'Quincke's siderosis,' 449
Quinine and chemiotaxis, 50
Quinsy, 393

Ranula, 226, 394
Rash in syphilis, 111
Ray-fungus, 116
Raynaud's disease, 30
Recklinghausen's disease, 691
Rectum, tuberculous ulceration of, 426
Recurrent fibroma, 139
Red and white softening, 659
Regeneration, 76
    of blood-vessels, 84
    of connective tissues, 78
    of epithelia, 76
    of gland, 83
    of lymphatics, 86
    of muscle, 82
    of nerve tissue, 87
Renal fibrosis, 546
    infarction, 535
Repair after inflammation, 89
    of bone abscess, 100
    of clean-cut wound, 90
    of inflamed pleura, 102
    of simple fracture of bone, 93
    of typhoid ulcer, 95
Resolution, 66
Retained testicles, 576
Retention cysts, 226
Retina, diseases of, 641
Rhabdomyoma, 174
Rhabdomyosarcoma, 174
Rheumatism, 358
    gonorrhœal, 362
Rheumatoid arthritis, 366
Rhinitis, chronic, 383
Rhinoscleroma, 383
Rickets, 341
'Rider's bone,' 169
Rodent cancer, 212
    ulcer, 210, 212
Round-cell sarcoma, 187
Rupture of cerebral vessels, 671
    of heart, 286

Saccharomyces albicans, 379
Saccular aneurysm, 301
'Sago spleen,' 17
Salpingitis, 595
Salivary calculi, 394
    glands, 394
Sarcinæ, 57
Sarcoma, 186
    alveolar, 194
    calcifying, 197
    carcinomatodes, 207, 620
    chondro-, 196
    deciduocellulare, 607
    distribution of, 204
    endothelioma, 201
    epulis, 205
    giant-cell, 190
    hæmangeio-, 203
    lymphangeio-, 203
    lympho-, 193
    melanotic, 25, 192
    mixed-cell, 190
    oat-cell, 190
    osteo-, 198
    osteoid-, 198
    psammoma, 193
    round-cell, 187
    spindle-cell, 189
Scar, 92
'Scavenging action' of leucocytes, 51
Schizomycetes, 56
Scirrhus, 222
    of pylorus, 404
Scleroses of spinal cord, 680
Sclerosis of bone, 101, 335
Scrotum, 580
Scurvy rickets, 345
Senile fibroses, 121
Sequestrum, 28, 72
Serous atrophy of heart, 283
Siderosis of kidney, 531
    of liver, 241, 449
Silver in kidney, 531
Sinus, 73
Skin, 623
    atrophy and hypertrophy, 623
    inflammations, 628

Skin, new-growths, 635
    pigmentations, 626
    vascular changes, non-inflammatory, 626
Skin-grafting, 77
Slough, 28, 72
Snuffles, 114, 336
Sodium biurate in gout, 360
Softening of brain, 659
Soft sore of penis, 571
Specific inflammation, 61, 105
    fevers, larynx in, 485
Spermatozoa in urine, 566
Sphacelus, 28
Spheroidal-cell carcinoma, 219
Spina bifida, 685
Spinal cord, 675
    atrophy of, 675
    central canal, diseases of, 684
    degenerations of, 675
    grey matter, affections of, 682
    meningitis, 677
    myelitis, 675
    scleroses, 680
    syphilis, 679
    tuberculosis, 678
    tumours of, 679
Spindle-cell sarcoma, 189
Spirilla, 57
Spleen, 318
    abscess of, 321
    'hardbake,' 319
    infarcts of, 321
    in malaria, 319
    in the anæmias, 319
    lardaceous change in, 16
    tuberculosis of, 320
Splenic anæmia, 255
Spleno-medullary leuchæmia, 252. (*See* Leucocythæmia)
Splenomegaly, 255
Splenules, 322
Spongy exostosis, 168
Spores, 56
Squamous-cell carcinoma, 208
Staphylococci, 57
Staphyloma, 639
Stenosis of œsophagus, 397
Stercoral ulcer, 425
Stomach, 398
    carcinoma of, 223, 402
    congestion of, 402
    hour-glass contraction of, 402
    in corrosive poisoning, 406
    inflammation of, 399. (*See* Gastritis)
    lymphadenoma of, 406
    post-mortem digestion of, 407
    sarcoma of, 405
Stomatitis, 379
    follicular, 380
    gangrenous, 380
Stools, abnormal conditions of, 430
Strangulated hernia, 412
Strawberry tongue, 387
Streptococci, 57
Stricture of intestine, 425, 428
    of urethra, 559
Sub-involution of uterus, 587, 606
Sudamina, 630
Suppuration, 67
    and lardaceous change, 17
Surgical kidney, 542
Sweating in arterial congestion, 40
Symmetrical gangrene, 30
Sympathetic nervous system, diseases of, 692
    ophthalmia, 644
Synechiæ, 640
Syphilis, 110
    and lardaceous change, 17
    caseation in, 111
    condylomata and mucous tubercles in, 112
    congenital, 114
    endarteritis obliterans in, 111
    gummata in, 112
    liver in congenital, 114
    of bone, 334
    of brain, 666
    of breast, 612
    of bronchi, 489
    of larynx, 484
    of liver, 457
    of lung, 519
    of lymphatic glands, 325
    of nose, 384
    of spinal cord, 679
    of testis, 575
    of uterus, 592
    post-tertiary phenomena in, 113, 115
    rash in, 111
    snuffles in, 114
    stages of, 110
    teeth in congenital, 115
Syphilitic cirrhosis, 464
    endarteritis, 308
        of cerebral vessels, 670
    ulceration of intestine, 425
Syringomyelia, 685

'TABBY-CAT striation,' 284
Tabes dorsalis, cord in, 681
Tænia mediocanellata, 433
    solium, 433
Teeth and gums, 389
    caries, 389
    in congenital syphilis, 115
Temperature in inflammation, 45
Tendons, 373
Tenosynovitis, 374
Teratoid tumours, 136
Teratoma, 231
Testes, 573
Threadworm, 433
Thrombi, canalisation of, 131
    fate of, 129

- Thrombi, varieties and formation of, 125
- Thrombosis, 125
  - conditions leading to, 127
- Thrombosis of cerebral sinuses, 658
  - vessels, 670
- Thrush, 379
- Thymus, 327
- Thyroid body, 527
- Tissue, granulation, 95
  - tension, 145
- Tongue, 386
  - in fever, 386
  - inflammation of, 388
  - new-growths in, 389
  - variations in size of, 387
- Tonsils, 391
- Tophi, 361
  - in auricle, 645
- Toxic anæmias, 251
- Toxins, 58
- Trachea, 481. (*See* Larynx)
- Tracheitis, 485
- Trachoma, 638
- Transitional carcinoma, 405
  - epithelium, 148
- Transverse myelitis, 676
- Traumatic aneurysm, 304
  - arthritis, 363
- Trichiniasis, 373
- Tropical abscess, 453
- Tubal nephritis, 536
  - acute, 538
  - contracted white, 539
  - secondary to chronic fibrosis, 541
  - subacute, 539
- Tubercle, miliary, 105
- Tubercles, mucous, in syphilis, 112
- Tuberculosis, 105
  - caseation in, 107
  - epithelioid cells in, 106
  - formation of vomica in, 107
  - lymphoid cells in, 106
  - of adrenals, 568
  - of bladder, 556
  - of bones, 337
  - of brain, 665
  - of breast, 612
  - of conjunctiva, 638
  - of Fallopian tubes, 598
  - of intestine, 418
  - of iris, 640
  - of joints, 363
  - of kidney, 544
  - of larynx, 483
  - of liver, 458
  - of lung, 514
  - of lymphatic glands, 325
  - of nose, 384
  - of skin, 632
  - of spinal meninges, 678
  - of spleen, 320
  - of testis, 573
  - of uterus, 592
- Tuberculous arteritis, 309
  - diseases of bone, 337
- Tuberculous meningitis, 655
  - pericarditis, 264
  - peritonitis, 437
  - ulceration of rectum, 426
- Tubo-ovarian cysts, 600
- Tubular adenoma, 179
- Tumours, 136. (*See also* New-growths)
  - classification of, 152
  - etiology of, 140
  - formation, theories of, 141
  - homologous and heterologous, 137
  - malignancy and non-malignancy, 138
  - malignant, carcinoma, 207
    - colloid, 224
    - columnar-cell, 215
    - duct, 218
    - rodent, 212
    - spheroidal-cell, 219
    - squamous-cell, 208
    - villous, 218
  - malignant, sarcoma, 186
    - alveolar, 194
    - calcifying, 197
    - chondro-, 196
    - endothelioma, 201
    - epulis, 205
    - giant-cell, 190
    - hæmangeio-, 203
    - lymphangeio-, 203
    - lympho-, 199
    - melanotic, 192
    - mixed-cell, 190
    - oat-cell, 190
    - osteo-, 198
    - osteoid, 198
    - psammoma, 193
    - round-cell, 187
    - spindle-cell, 189
  - non-malignant, of connective tissues, 161
    - angeioma, 169
    - chondroma, 166
    - fibroma, 161
    - glioma, 173
    - lipoma, 165
    - myxoma, 162
    - osteoma, 167
  - of epithelial tissue, 157
    - callosity, 157
    - keratoma, 158
    - papilloma, 157
  - of glandular tissue, 179
    - adenoma, 179
    - lymphoma, lymphadenoma, 183
  - of muscular tissue, 174
    - leiomyoma, 176
    - rhabdomyoma, 174
  - of nervous tissue, 178
    - neuroma, 178
  - typical and atypical, 137
- Typhoid fever, eruption in, 629
  - larynx in, 485
  - thrombosis in, 128
  - vitreous change in, 22

Typhoid ulcer of intestine, 416
  repair of, 95

ULCER, 71
  duodenal, 416
  fæcal, 425
  gastric, 399
  malignant, 74
  perforating, 635
  repair of typhoid, 95
  rodent, 210, 212
  tuberculous, of intestine, 418
  typhoid, of intestine, 416
Ulceration, 67
  malignant, 74
  of new-growths, 151
  syphilitic, of intestine, 425
  tuberculous, of rectum, 426
Ulcerative colitis, 422
  endocarditis, 270
Umbilical vein after birth, 9
'Undefended spot,' 293
Ureters, 552
Urethra, 558
  gonorrhœa, 558
  stricture, 559
  vascular caruncle, 559
Uric acid infarction, 533
Urinary apparatus, malformations of, 559
  bladder, 554
    atrophy and hypertrophy, 554
    inflammation, 555
    new-growths of, 556
Urine, abnormal constituents of, 562
  bacteria, 566
  Bilharzia hæmatobia, 566
  blood, 564
  calculi, 562
  casts, 565
  crystals, 567
  pus, 564
  spermatozoa, 566
Urticaria, 631
Uterine fibroids, 177
  calcification of, 23
Uterus, 587
  atrophy, 587
  hypertrophy, 587
Uterus, inflammation, 588
  in pregnancy, 8
  new-growths, 593

VACUOLATION, 450
Vaginitis, 586
Valvular endocardium, 266
Varicocele, 580
Varicose veins of œsophagus, 398
Varix, 310
Vascular caruncle, 559
Vater, ampulla of, 475
'Vegetations' in valvular endocarditis, 268
Vegetative endocarditis, 268
Veins, 310
  in chronic venous congestion, 39
  new-growths in, 313
Venom, 59
Venous congestion, 37
  nævi, 171
Vesicles, 629
Vesiculæ seminales, 580
Vibrio, 57
Villous carcinoma, 218
    of kidney, 550
  papilloma of bladder, 556
Virchow, theory of tumour formation 141
Vitiligo, 25, 626
Vitreous change, 22
Volvulus, 413
Vomica, formation of, 107
  in lung, 518
Vulva, diseases of, 584

WANDERING cells. (*See* Leucocytes, etc.)
Warts, 140, 158
Wasting in diabetes mellitus, 10
Waxy change, 16
Whitlow, 374
Worms, intestinal, 433
Wound, repair of clean-cut, 90

ZENKER'S degeneration, 22

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